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THE RATIONALE OF ANASTOMOSIS OF THE RIGHT AURICULAR APPENDAGE TO THE PULMONARY ARTERY IN THE TREATMENT OF TRICUSPID ATRESIA

APPLICATION OF THIS PROCEDURE TO A CASE OF COR TRILOCULARE

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PALLIATIVE surgery by means of the Blalock[1] or Potts[2] type of anastomosis has been less satisfactory for tricuspid atresia than for the tetralogy of Fallot. An analysis of the first 1,000 cyanotic cardiac patients to be operated upon by Blalock and his group showed that 21 per cent of 62 patients with tricuspid atresia died at or shortly after operation, with a total mortality of 26 per cent eight months postoperatively.[3] In the series reviewed by Sommers and Johnson,[4] more than two-thirds of all patients with tricuspid atresia died before one year of age because of congestive heart failure and anoxia, whether or not surgery had been performed; in 4 infants, shunts of the types just described had been constructed with no striking increase in longevity.

On Nov. 15, 1954, in the Forum on Fundamental Surgical Problems of the American College of Surgeons, a new surgical approach to the treatment of atresia of the tricuspid valve was described by Warden, DeWall, and Varco.[5] They performed an anastomosis between the tip of the right auricular appendage and the main pulmonary artery in dogs with suture-obliteration of the orifice of the tricuspid valve. Certain theoretical advantages were postulated for this procedure, in contrast to the extracardiac shunts of the Blalock or Potts type. Utilization of the pumping action of the right auricle in propelling the systemic venous blood into the pulmonary circulation, and avoidance of recirculation of blood already partially oxygenated, were considered to be factors in support of this concept.

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The attention of the cardiovascular group at this hospital became focused on this situation because of a desperately sick, intensely cyanotic infant in whom a clinical diagnosis of tricuspid atresia was made. Extensive conference deliberation, abetted by the demonstration in the laboratory of the technical facility with which such an anastomosis may be constructed in the normal dog, led to a decision to attempt this anastomosis in the case under consideration, provided certain physiologic and anatomic conditions were substantiated at exploratory thoracotomy. Although the operation was unsuccessful, and a cor triloculare was found at autopsy, the total experience has provoked a critical analysis of the problem.

CASE REPORT

D. P., an intensely cyanotic 4-month-old white boy, weighing 9 pounds, was transferred to the Montefiore Hospital from the Staten Island Hospital by Dr. Oscar Race and Dr. J. Silverman on Nov. 18, 1954 (Admission No. 69742). Birth weight was 7 pounds, and cyanosis appeared promptly. The constant administration of oxygen became practically obligatory following the onset of an upper respiratory infection on November 13. On

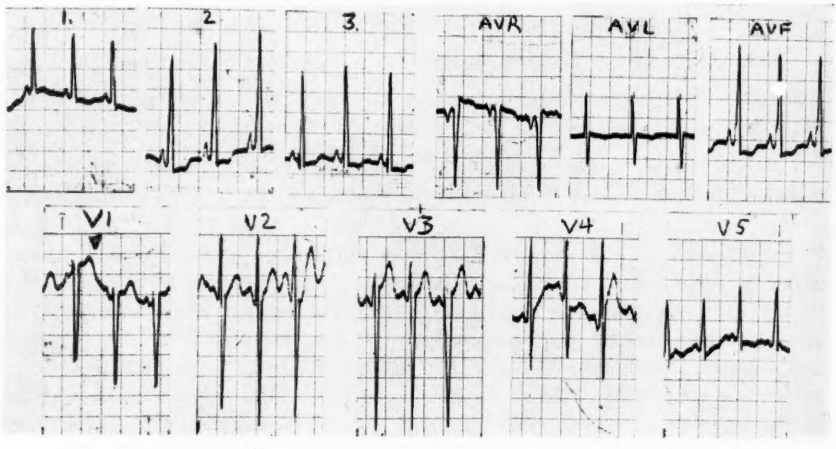

Fig. 1.—Electrocardiographic tracings showing absence of right ventricular preponderance (see text).

admission here, he was afebrile and grossly underdeveloped, but not dyspneic, and had no clubbing of the fingers or toes. There was no distention of the veins in the neck, and the lungs were clear. The heart was moderately enlarged, and there was a short rough systolic murmur over the second and third interspaces, to the left of the sternum. All heart sounds were described as being of normal quality, including the pulmonic second sound. The liver edge was felt 2 fingerbreadths below the right costal margin, and there was no edema of the trunk or extremities. The presence of frontal bossing and a widely open anterior fontanel suggested a mild hydrocephalus in addition to congenital heart disease.

The hemoglobin was 14 Gm. per cent, with an erythrocyte count of 5.09 million. The electrocardiogram showed absence of right axis deviation in the standard leads, an absent R wave in Lead AVR, and an extremely small R wave in Lead V_1 (Fig. 1). These findings are distinctly abnormal at this age and indicate left ventricular enlargement. Roentgenograms and cardiac fluoroscopy revealed a picture strikingly similar to that of tetralogy of Fallot. The pulmonary vascularity was diminished. The main pulmonary artery segment showed a

concavity, and the blunting, rounding, and elevation of the lower left cardiac border in the posteroanterior view suggested the appearance of the right ventricle as commonly seen with the tetralogy. The left anterior oblique position showed what appeared to be a small left ventricle, a mildly enlarged inflow tract of the right ventricle, and a normal-appearing right atrium (Fig. 2).

The diagnosis of tricuspid atresia was based on the association of severe cyanosis with the electrocardiographic rather than the roentgenographic features. During the 20-day period of hospitalization, there was progressive deterioration in the infant's condition and he experienced several almost lethal episodes of severe dyspnea with accentuation of cyanosis.

An operation was undertaken on Dec. 8, 1954. Preoperative medication consisted of morphine sulfate, 1/60 of a grain, and scopolamine bromide, 1/600 of a grain. Under satisfactory general anesthesia of vinyl ether and oxygen by Dr. Edith Kepes, an intratracheal tube was passed and the child was placed in a tub of ice and water for 12 minutes until his temperature reached 90° F. During the operation his temperature drifted over a 25-minute period to 82° F., where it remained for 35 minutes and he was carried in a light

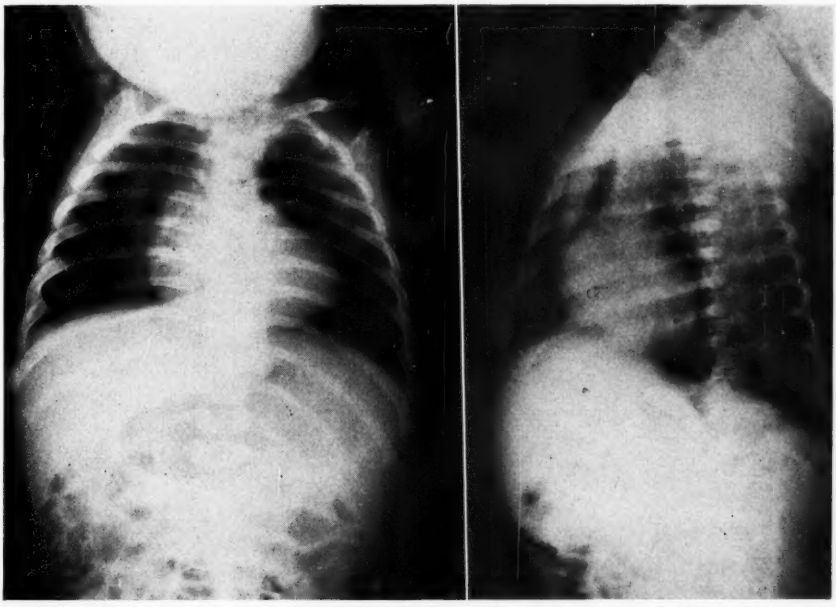

Fig. 2.—Posteroanterior and left anterior oblique chest roentgenograms, suggesting tetralogy of Fallot (see text).

plane with high concentrations of oxygen. With the child in the supine position, the right pleural cavity was entered through a submammary incision traversing the third interspace and transecting the sternum. The incision was extended across the left anterior thoracic wall and the left pleural cavity was entered through the third interspace for additional exposure (Fig. 3). The lungs appeared normal, there were no adhesions, and no increase in vascular collateral channels in the mediastinum. The thymus extended low onto the anterior surface of the pericardium and was mobilized and retracted with traction sutures. The pericardium was incised vertically, anterior to the right phrenic nerve, and a horizontal T-extension made overlying the region of the base of the heart toward the left phrenic nerve. The pericardial flaps were held apart with traction sutures. The right auricular appendage

was a dense blue in color, and both it and the right auricle were considerably enlarged and moderately tense. The superior vena cava was in the normal relationship, as was the aorta, which measured 12 mm. in diameter at its base. The main pulmonary artery was hypoplastic, measuring 6 mm. in diameter at its origin, and appeared to arise from a rudimentary right ventricle (Fig. 4). The small pulmonary artery appeared collapsed and extremely soft. There was no palpable thrill to suggest either a patent ductus arteriosus or a pulmonary valvular stenosis, and the pulmonic cusps were not rigid or thickened.

During this exploration the cardiac action was extremely erratic, periodically becoming very slow and irregular, and speeding up when warm saline was sprayed over the heart. The systolic blood pressure fell from 80 to 50 mm. Hg. During periods of better function, direct pressure measurements were obtained sequentially from the right auricular appendage and the main pulmonary artery, and recorded on a multichannel electronic recording apparatus.* The preliminary report indicated that the pulmonary arterial mean pressure was 11 mm. Hg, in contrast to 7 in the right auricle. Oxygen saturations of the blood, taken at the same time as the pressures, were determined to be 22.5 per cent from the right auricle and 27.5 per cent from the pulmonary artery, as measured on a Waters-Conley oximeter. The arterial oxygen saturation in the ascending aorta was 25 per cent, initially, and 32 per cent from the aortic arch, 12 minutes later. Because of the child's poor and variable condition, these data were of qualified value only, other than to point up what appeared to be a lack of pulmonic blood flow.

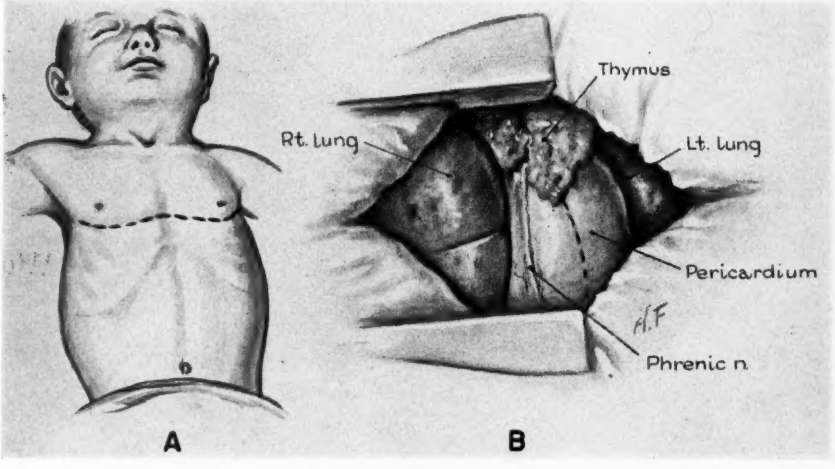

Fig. 3.—Diagram of operative position, incision, and exposure.

Since the clinical state of the patient precluded accurate evaluation of the pressure gradient between the pulmonary artery and right auricle, and no patent ductus arteriosus had been found, it was elected to attempt an anastomosis between the right auricular appendage and the pulmonary artery. The sulcus between the origin of the pulmonary artery and the aorta was dissected, mobilizing the first portion of the pulmonary artery. A Potts type of curved multitoothed clamp was applied over the base of the pulmonary artery in an attempt partially to occlude this; a Satinsky clamp was placed over the mid-portion of the right auricular appendage, and the tip of the appendage was amputated (Fig. 5). At this point, with a body temperature of 84.5° F, the heart again slowed considerably, went into cardiac arrest, and gave only an occasional beat despite vigorous attempts at resuscitation, including continuous rhythmic cardiac compression, intermittent inflation of the lungs,

*Manufactured by Electronics for Medicine, Inc., New York City.

intracardiac injections of epinephrine and calcium chloride, and rewarming with intrathoracic hot saline to 95° F. As soon as the heart had slowed, the clamp had been removed from the pulmonary artery and the lungs had been expanded.

An effective beat could not be re-established, but the heart was still contracting unpredictably when it was elected to complete the anastomosis in the hope that an increased

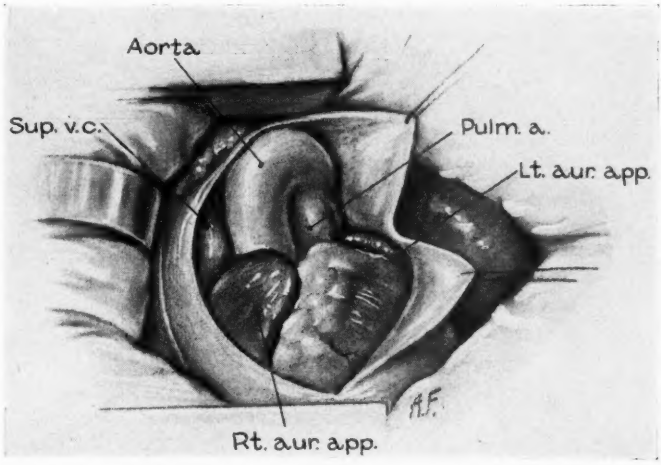

Fig. 4.—Pericardium opened, showing hypoplastic pulmonary artery.

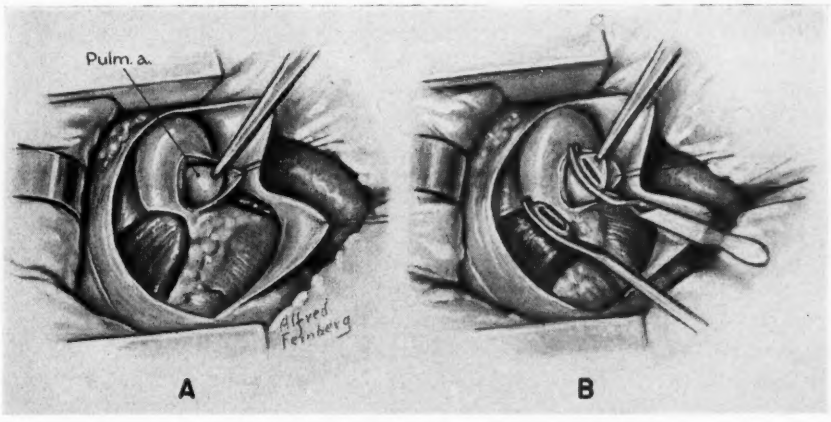

Fig. 5.—Preparation of pulmonary artery and right auricular appendage for anastomosis.

pulmonary blood flow might provide the possibility of survival. Trabeculae near the tip of the right auricular appendage were divided. A finely ground, thin-walled, multitoothed bulldog clamp was applied over the base of the pulmonary artery in such a way as to leave an adequate lumen. A 5 mm. vertical incision was made in the anterior wall of the pulmonary artery between the jaws of the partially occluding clamp. An anastomosis was constructed between the tip of the right auricular appendage and the incision in the pulmonary artery with a continuous suture of No. 5-0 Deknatel braided silk on a curved Atraumatic needle. The

anastomosis was accomplished without difficulty, since it was possible to bring the distended and enlarged right auricular appendage over to the pulmonary artery with no tension or distortion (Fig. 6). Following removal of the clamps, cardiac resuscitation still could not be achieved. It was felt that the final precipitating cause of death may have been the short period of occlusion of the pulmonary artery superimposed on a state of severe anoxia in a badly crippled heart.

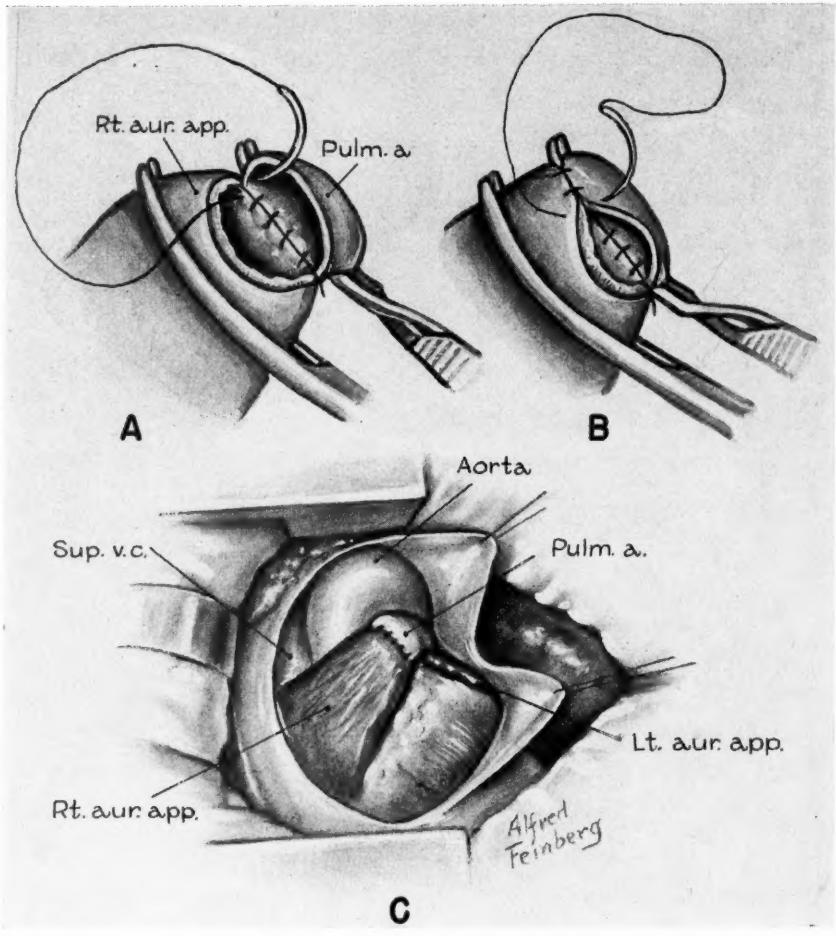

Fig. 6.—Technical details of anastomosis.

At autopsy there was found a cor triloculare with a large single ventricle and a rudimentary conus of a right ventricle. Both auricles communicated freely with the dilated, hypertrophied common ventricle, by a large mitral and a rudimentary tricuspid valve. There was hypoplasia of the pulmonary artery and the pulmonic valve was bicuspid. There was a small, probe-patent foramen ovale; the ductus arteriosus was obliterated. No evidence of congestive heart failure was found. It was felt that the common ventricle represented both

the left and right ventricles with no evidence of septation other than at the site of one of the papillary muscles. Permission to examine the brain was not obtained, so that the question of early hydrocephalus could not be resolved.

DISCUSSION

From the onset, it was apparent that there were certain important differences between the provocative experimental situation of Warden, DeWall, and Varco and the human case of cyanotic congenital heart disease, of which tricuspid atresia might be a component. In a case of true tricuspid atresia, the presence of an interauricular septal defect is obligatory for survival. The maldevelopment of the right ventricle, which appears to be the primary defect, may also involve the main pulmonary artery.[6] The blood reaching the lungs does so largely by way of a patent ductus arteriosus, bronchial arteries, or collateral mediastinal vessels.

The success of an anastomosis designed to carry blood from the right auricle to the pulmonary artery depends upon a pressure gradient in the proper direction. In a true tricuspid atresia, with a hypertrophied, hypertensive right auricle, this gradient would almost certainly be present and demonstrable unless masked or reversed by the additional presence of a patent ductus or ventricular septal defect. Cases of tricuspid atresia may occur, however, with deep cyanosis by virtue of a large interatrial septal defect without having enough reduction of pulmonic flow to provide the necessary pressure differential.

The association of left ventricular preponderance in the electrocardiogram with the clinical and radiographic features of Fallot's tetralogy is usually indicative of tricuspid atresia, and in infancy the electrocardiographic evidence is considered to be more reliable than the roentgenographic interpretation. Others have also noted, however, that a similar electrocardiographic pattern may be found in a variety of cyanotic lesions characterized by a common ventricle.[7] The unreliability of this finding as pathognomonic of tricuspid atresia has not been widely appreciated and resulted in the diagnostic error in the present case.

It had been hoped that one might be able to confirm the clinical diagnosis by means of differential pressure and oxygen determinations during the operation. Actually this patient's condition prevented definitive analysis, so that the decision to proceed was based on the clinical data, and the hope that an increased flow of blood to the lungs might improve the possibility of survival. The demonstration of a cor triloculare at autopsy indicates that a Blalock type of shunt would probably have been preferable, as suggested by Taussig,[8] although an atriopulmonic shunt might have functioned in view of the markedly restricted pulmonic blood flow caused by the rudimentary right ventricular conus.

At the time of commencing to construct such a shunt, it would be preferable to prepare the right auricular appendage before interfering with the main pulmonary artery. If possible, a partially occluding clamp should then be applied to the pulmonary artery. If this is not feasible and total pulmonary arterial obstruction is necessary, and/or cardiac arrest should ensue as it did under hypothermia in this instance, the procedure of choice should be an immediate and rapid anastomosis, reserving efforts at resuscitation until this has been completed.

Despite the initial appeal of the atriopulmonic shunt in the treatment of tricuspid atresia, and the comparatively poor results achieved by other methods, there are several factors which suggest that the usefulness of this new procedure will probably be quite limited. The presence of a large interatrial defect may conflict substantially with the amount of blood leaving the right auricle by way of the new shunt. Should auricular failure or fibrillation occur, the pumping action would become ineffectual. If left heart failure or mitral valvular disease were to develop, the pressure gradient might reverse. Acute or chronic pulmonary disease might obliterate the pressure gradient. And, with any significant degree of hypoplasia of the main pulmonary artery, it is doubtful whether a satisfactory anastomosis could be constructed or whether the low-power thrust of the auricle could move an effective volume of blood into the narrowed channel. None of these situations would give cause for similar concern following a Blalock or Potts operation. In addition, although Warden, DeWall, and Varco have observed that the right auricle may fulfill the pumping requirements of the right heart under conditions of experimental abolition or massive infarction of the right ventricle, long-term survival studies are not yet available to indicate how long the auricle could maintain its pumping potential against the elastic recoil of the pulmonary arterial tree. The two-month survival period recorded by Rodbard and Wagner[9] in dogs with anastomoses of right auricle to pulmonary artery, but without obliteration of the tricuspid orifice, suggests that longer periods of observation might be of considerable value.

Many of the problems presented in this discussion may not be insurmountable. The implication of these considerations and this case report is that further investigation will be necessary before one may state whether or not anastomosis of the right auricular appendage to the pulmonary artery may be beneficial in a case of tricuspid atresia. The circulatory by-pass of the right heart described by Glenn and Patino,[10] anastomosing the azygos vein to the right pulmonary artery, and the anastomoses between the venae cavae and the pulmonary artery referred to by Shumacker[11] represent provocative experiments in this direction.

SUMMARY

1. A critical analysis is presented of the rationale of right auricular-pulmonary arterial anastomosis in the treatment of tricuspid atresia.

2. An anastomosis between the right auricular appendage and the main pulmonary artery was performed in a cyanotic infant suspected of having tricuspid atresia.

3. At autopsy a cor triloculare was found with a rudimentary right ventricular conus causing a marked obstruction to pulmonary arterial blood flow.

4. The presence of a pressure gradient from right auricle to pulmonary artery should be demonstrated at operation if this type of shunt is under consideration.

5. The absence of right ventricular preponderance in the electrocardiogram of a cyanotic infant with the radiologic configuration of a tetralogy of Fallot is not pathognomonic of tricuspid atresia.

We gratefully acknowledge the generous suggestions of Dr. Louis Leiter in evaluating this material.

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DISCUSSION

DR. HARRIS B. SHUMACKER, Indianapolis, Ind.—With reference to the paper Dr. Hurwitt presented, I thought you might be interested in several other experiences with right heart by-pass. Unfortunately, they all ended fatally. We have not felt justified in using this operation in cases of tricuspid atresia, for our experience with the shunt operation of Dr. Blalock in the treatment of this condition has been good. We have, however, done a partial or total by-pass in 3 children with conditions with which we have had no success with other methods of treatment. One was a very sick child who had truncus arteriosus with pulmonary hypertension and large pulmonary trunks coming off the common one. In this case and in one case with complete transposition we simply performed a superior vena cava-right pulmonary artery end-to-end anastomosis. Both children succumbed some eight to fifteen hours later. We subsequently treated 1 patient with complete transposition of the great vessels with ventricular septal defect and without atrial septal defect by total right heart by-pass. Since the pulmonary trunk was posterior we could not directly anastomose the right atrial appendage to it and had to interpose a graft. We then closed off the tricuspid valve by mattress sutures guided in place with a finger inside the atrium, and finally we completely eliminated blood flow from the right ventricle into the pulmonary artery by sutures. We were pleased to observe that at the completion of the procedure the child was well colored and had excellent peripheral pulses and excellent blood pressure. This child, unfortunately, died rather suddenly about six or eight hours later. Study at post mortem failed to explain the mechanism of death. The peripheral circulation had been excellent up until the end. The autopsy confirmed the complete transposition, the large ventricular septal defect, the intact atrial septum, and the complete by-pass of the right heart. This experience does demonstrate that, at least for a period of hours, the human heart can function with the right side circumvented completely.

DR. HERBERT E. WARDEN, Minneapolis, Minn.—I rise for a twofold purpose and will be very brief. First, I want to congratulate Dr. Hurwitt and his group on their presentation and their courage in attempting surgical amelioration of this dismal form of congenital heart disease. Second, I want to respond to the inquiry regarding the results of our long-term survivors. The entire group of animals that was reported last fall, in which a tricuspid obstruction had been produced followed at a later stage by a right auricular pulmonary artery anastomosis and complete occlusion of the tricuspid valve, is alive; the longest of which is two years, the shortest six or seven months. We have felt, as was suggested here this morning, in view of the fact that most forms of congenital tricuspid atresia have associated abnormal intracardiac shunts, that the method warranted further evaluation in the presence of such a defect. We are attempting to do this by first producing an artificial ductus and, at a second operation, by suturing the tricuspid valve and at the same time creating an interatrial septal defect. These animals will then be treated by a corrective right auricular pulmonary artery shunt. This group is being studied now and it is too early to make any conclusive report.

AUTOGENOUS THORACIC AORTA GRAFTS OF PERICARDIUM AND NYLON NET USING A THROMBIN-FIBRINOGEN COAGULUM

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TODAY, a number of congenital, traumatic, and degenerative lesions that involve the thoracic aorta may be adequately resected; but the problem of finding an ideal long-term replacement for the excised aortic tissue remains to be solved. The lack of an available autogenous artery has resulted in widespread investigation to find an aorta substitute using homologous and heterologous vessels, diverse plastic prostheses, and ingenious combinations of nonvascular tissues. Certain undesirable features associated with homologous grafts, not seen in autogenous grafts, and the additional problems associated with the maintenance of an aortic vessel bank, stimulated a search for a simple practical method of making aortic grafts from a suitable body tissue that would be readily available and expendable at the time of thoracotomy. This paper will outline the method developed in dogs to meet these needs by making thoracic aorta grafts from autogenous pericardium, nylon net, and a coagulum of thrombin and fibrinogen.

MATERIALS AND METHODS

Mongrel dogs weighing from 18 to 65 pounds were used. Intravenous pentobarbital sodium (Nembutal) was used for anesthesia and intermittent positive pressure administered by a M.S.A. demand pneophore apparatus. The left hemithorax was exposed through the fifth interspace. A large sheet of pericardium was removed and trimmed free of adhering fat. The aorta just distal to the ligamentum arteriosum was selected as the site for insertion of the graft because it was thought that, in this location, the graft would be subjected to maximum stress.[1] The left subclavian artery and distal aorta were mobilized and a variable number of intercostal arteries divided. The diameter of the aorta was carefully measured with calipers and a glass suture tube or test tube of appropriate size selected for fashioning the graft. Except for certain initial short-length grafts in which the aorta was only divided, a segment of aorta approximately three-fourths the length of the graft was usually resected.

A siliconized polythene shunt was devised that protected the dog from any untoward effects of aortic cross-clamping. The proximal flanged end was tied into the left subclavian artery, and the distal end was quickly inserted into the descending aorta through a small incision and held there by an outside constricting double loop of oiled umbilical tape. The intervening aorta was excised between Potts' coarctation clamps.

Nylon net,* of the type described by Vargas and Deterling,[2] was selected to prevent dilatation and aneurysm formation which had been shown to occur when

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*Supplied by Ethicon Suture Laboratories.

pericardium was used as a graft in the thoracic aorta.[3, 4] To eliminate certain disadvantages associated with Vargas and Deterling's method of rolling out a preformed nylon net tube over a graft at the completion of the anastomoses and anchoring it by sutures, a method was developed for causing the pericardium and nylon net to adhere together as one tissue. Topical thrombin* and fibrinogen† were combined to form a sticky, physiologic coagulum. The outer

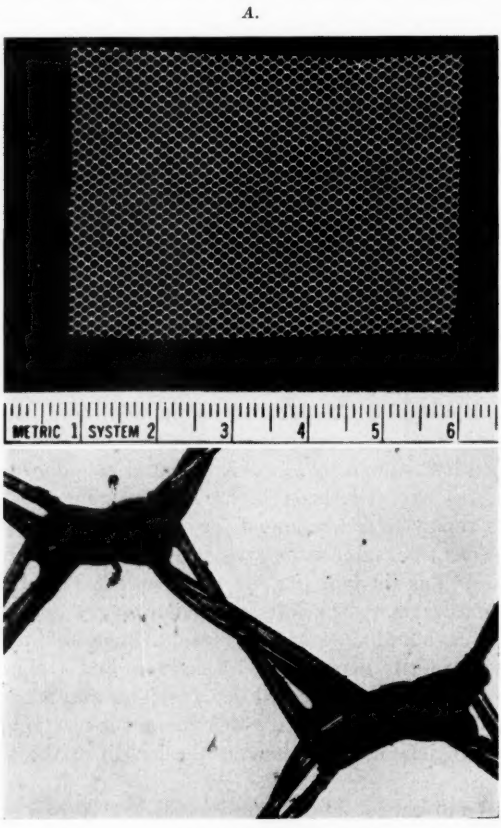

Fig. 1.—Nylon net. *A*, Gross appearance. *B*, Photomicrograph magnified ×70. Note knotting of fiber junctions.

surface of the pericardial sheet was first covered with a layer of thrombin solution (2,000 NIH. units per c.c.). A moderately heavy layer of preserved fibrinogen powder was then sprinkled on this surface. A rectangular piece of nylon net, fashioned to appropriate size, was immediately placed on this coated pericardial surface. Within several minutes the fibrinogen was in solution; the net and pericardium became adherent and could be handled as one tissue. These

*Thrombin, topical (bovine); supplied by Parke, Davis & Company.
†Fibrinogen (human), Parenogen; supplied by Cutter Laboratories, Berkeley, Calif.

two were then wrapped around the oiled glass tube, the inner pericardial surface facing the tube and the net facing the outside. By means of a continuous mattress suture of No. 5-0 arterial silk, reinforced by an outer whipping suture, a cylinder was formed that could be easily slipped off the glass tube, ready for use.

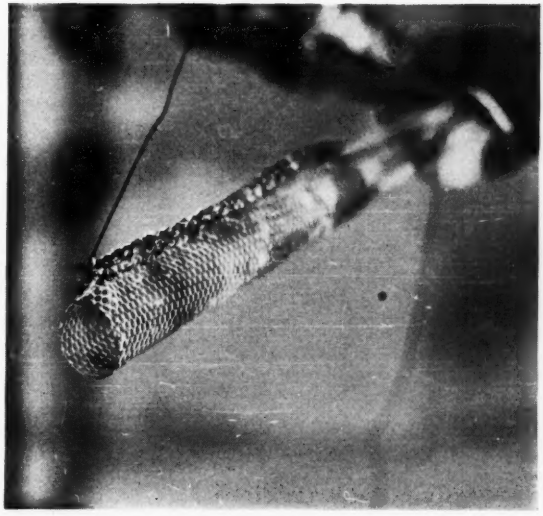

Fig. 2*A*.—Oblique end view of newly made graft partially off glass tube.

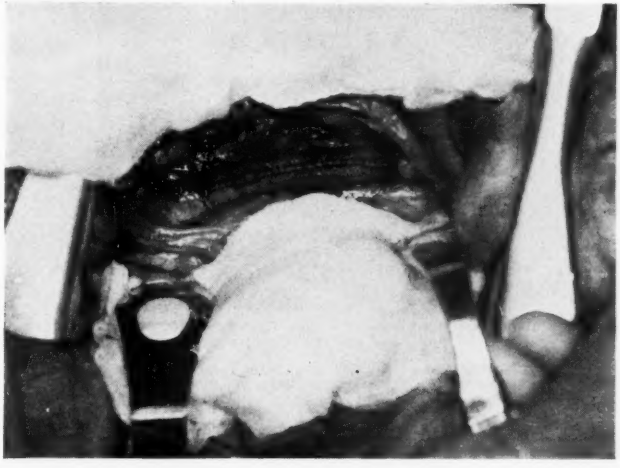

Fig. 2*B*.—Operation view of graft following anastomoses to aorta, graft longitudinal suture cuff seen end on.

Grafts varying in length from 2 to 7 cm. and in diameter from 8 to 15 mm. were anastomosed to the aorta by interrupted everting mattress sutures of No. 5-0 arterial silk. The occasional slight tendency of the net and pericardium

to separate at the end of the graft when the suture needle was inserted was easily controlled as one became familiar with handling the graft. Special care was taken to insert the suture needle behind at least one crossing of the nylon net fibers. Because these nylon fiber junctions were knotted, raveling was prevented and a sound anastomosis ensured. A cuff of a graft approximately 1 to 2 mm. long was usually everted.

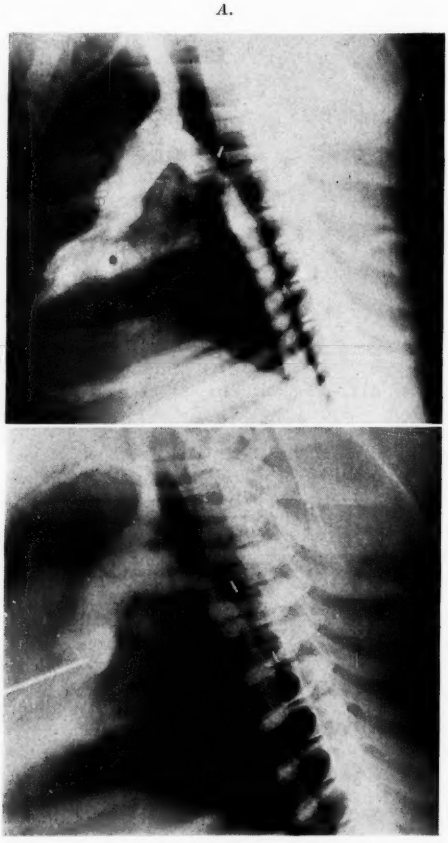

Fig. 3.—Representative aortograms. Silver clips placed adjacent to graft-aorta anastomoses at surgery. *A*, Five months; *B*, eight months.

Upon completion of the anastomoses, the shunt was removed by suturing the distal aortic incision and ligating the subclavian artery at the aortic arch. Two silver Cushing brain clips were placed on adjacent tissue to identify the superior and inferior extent of the graft for later x-ray. The dogs received daily penicillin for approximately one week and were followed postoperatively by palpation of femoral pulses, chest x-rays and aortograms, reoperation, and necropsy. Gross specimens were photographed and histologic sections appropriately

stained by hematoxylin and eosin, van Gieson, Verhoeff (elastic), and special histochemical techniques and stains to be mentioned.

Physical limitations made it necessary to develop a method of aortography that would eliminate the need for arterial cutdown and catheterization. In the right lateral position, the point of maximum cardiac impulse was usually palpated about the left fourth or fifth interspace approximately 4 to 6 cm. posterior to the sternum. A No. 18 needle, mounted on a 10 c.c. syringe, was introduced at this site at approximately a 45 degree angle, posteriorly and

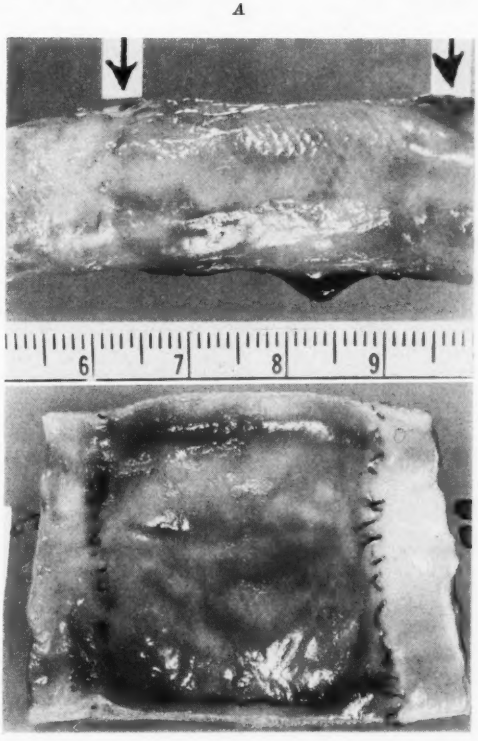

Fig. 4.—Five-month postoperative graft-aorta specimen. *A*, External appearance. Lung has been stripped away, net fibers partially visible. Arrows indicate anastomoses between graft and aorta. *B*, Same specimen opened showing glistening graft lining and thickened graft wall.

medially, until it entered the left ventricle. This position was confirmed by drawing back bright red blood, and then 10 c.c. of 35 per cent Diodrast was quickly injected. Eight exposures, at one-half second intervals, were made on a Sanchez-Perez seriograph. Occasionally, the right heart was accidentally entered and the aortogram would be repeated immediately. A number of animals had two or more aortograms without untoward effects. Recently, Smith and his associates have reported the use of a transventricular technique, stating preference for the subxiphoid approach.[6]

RESULTS

Thirty-five dogs included in this study were autopsied at postoperative periods from one day through eleven months. Initially, several dogs died in the immediate postoperative period from the effects of aortic cross-clamping before the shunt was devised. Although their grafts were examined, they were not included in this group. Necropsy was performed at regular short

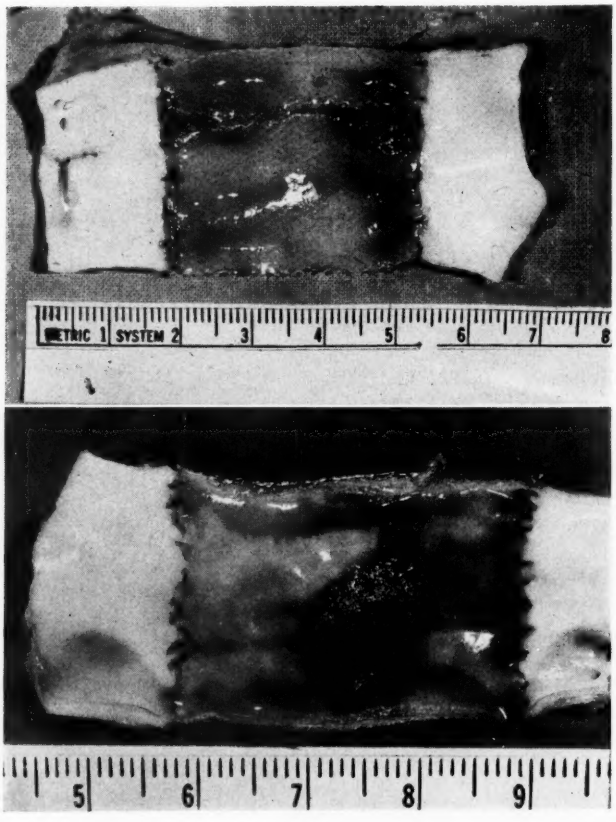

Fig. 5.—Graft and aorta opened longitudinally. *A*, smooth layer lining graft, redness disappearing; one week. *B*, Mural thrombus in central graft with early yellow and orange discoloration along periphery of thrombus; four months.

intervals during the first three weeks and thereafter at approximately monthly intervals. Of the total, 2 dogs died from dehiscence of the anastomotic suture line, both secondary to adjacent infection; 1 at eight days due to a localized abscess, and the other at forty-seven days due to infection from a retained surgical sponge. Another died at three months from mesenteric and peripheral emboli originating in a thrombus at a technically faulty distal anastomosis. Several dogs dying of unrelated causes at later periods were also included.

The majority of the dogs were alive and active at the time of elective reoperation and autopsy.

Dogs past the first postoperative month had an aortogram before elective sacrifice and a number had additional aortograms during their postoperative course. No graft showed significant dilatation or constriction, although several displayed some narrowing at the sites of anastomoses. In over 60 intracardiac aortograms there was no instance of extensive bleeding, myocardial damage, or death directly attributable to the method. The elastic properties of the nylon

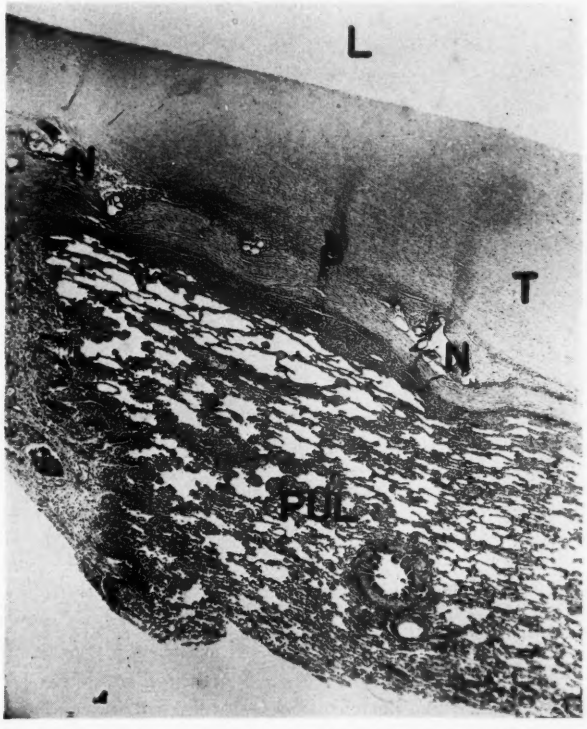

Fig. 6.—Photomicrograph of central area of graft with organizing mural thrombus; one and one-half months. Thrombus intimately adherent to pericardium and developing smooth surface. It blended gradually into pseudointima covering graft. The thrombin-fibrinogen coagulum has been replaced by fibrous tissue. *L*—lumen, *T*—thrombus, *P*—pericardium, *N*—site of nylon net (fragmented during preparation of specimen), *PUL*—adherent pulmonary tissue. (hematoxylin and eosin stain; 32 mm. micro tessar.)

net allowed the graft to have a certain amount of expansile pulsation observed at the time of the original operation and also at reoperation months later. This was always less pronounced than that seen in the proximal aorta. Adjacent tissue and lung soon became adherent to the graft and occasionally direct vascular communications were observed.

By four to six hours postoperatively, a red, patchy deposition of blood elements could be seen on the surface of the pericardium. During the next several days, this usually progressed to a velvety layer of blood cells and fibrin that could be partially scraped off the pericardium with a fingernail. At

the end of one week, this layer had become a paler, rather homogeneous, fibrinous coagulum with a smooth surface that blended with the intima advancing from the aorta. By two weeks, this pseudo-intima was becoming more fibrinous with a surface layer that assumed an intimalike function in later weeks.

The thrombin-fibinogen coagulum between the pericardium and nylon net was invaded by new capillaries at the end of one week following an earlier period of cellular infiltration. By two weeks, this substance was partially replaced by fibrous tissue binding the nylon net to the pericardium. A similar fibrous

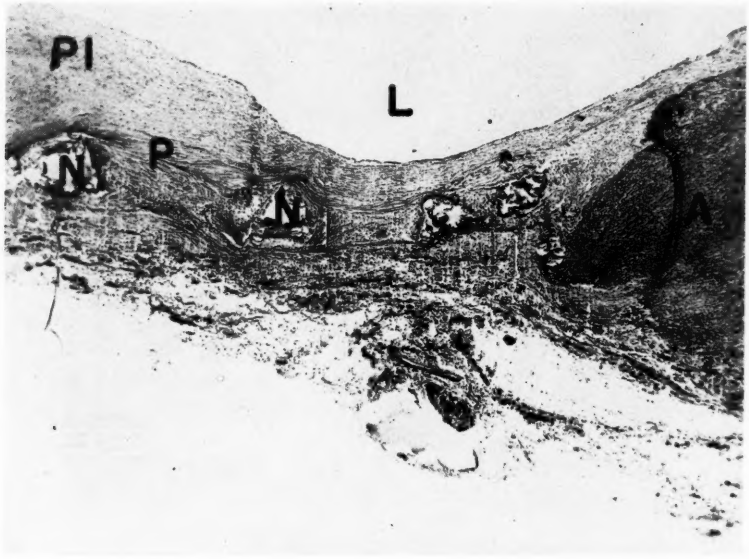

Fig. 7.—Photomicrograph of aorta-graft junction; eight months. Note firm union of aorta and graft and blending of intima from aorta with pseudointima of the graft. *A*—aorta, *P*—pericardium, *PI*—pseudointima, *N*—site of nylon net (fragmented in preparation of specimen), *L*—lumen (hematoxylin and eosin stain; 48 mm. micro tessar.

reaction occurred outside the nylon which contributed to the progressive thickening of the graft wall. The pericardium maintained its normal appearance, although in two grafts it underwent a moderate but temporary swelling between the second and fifth postoperative days. By eight to ten months the pericardium appeared to blend with the adjacent fibrous tissue.

Mural thrombi were rather surprisingly common. They were most frequently located in the central area of the graft and on surface irregularities. These thrombi usually lost their red color and blended with the surrounding pseudointima when examined in later months. Yellow and orange stains and patches were also observed in a number of grafts.

DISCUSSION

The thrombin-fibrinogen coagulum was effective in holding the nylon and pericardium together. It appeared to be well tolerated by the host, becoming replaced by fibrous tissue (further detail on the uses of topical thrombin and

fibrinogen is to be published). The nylon net was an effective elastic support that prevented dilatation of the graft, allowed free ingrowth of an adjacent vascular supply, and permitted a sound anastomosis between the graft and aorta. The pericardium maintained its normal appearance although it seemed to undergo swelling or mild degeneration during the first several days, possibly reflecting an interval until it gained a new blood supply. Its surface usually became coated, to a variable degree, by precipitated blood elements which formed a rather homogeneous coagulum that underwent fibrinous change and assumed the function of an intima. This layer, despite its varying thickness in different grafts as well as in different areas of the same graft, blended smoothly with the aortic intima. It appeared that the intima, advancing from each end of the host aorta, seldom completely spanned the graft. This left the more central portions of the graft covered by the blood elements which adapted to the function of an intima or progressed to form a mural thrombus. Flattened mural thrombi also occurred in irregularities and depressions in the graft as if trying to fill in such areas in an effort to form a more uniform and streamlined lumen. These mural thrombi usually lost their granular appearance and eventually developed a smooth surface that blended in with the adjacent pseudo-intima.

By two to three months, yellow and orange stains and patches could be seen that have been referred to as cholesterol degeneration of the pericardium.[3, 4] In this study, this was observed almost invariably in association with mural thrombi which stimulated a more detailed examination of the phenomenon. In older grafts, these yellow and orange areas tended to persist as the mural thrombi were losing their identity by organization and functional adaptation. If a new layer of blood elements became deposited on the surface of the organizing thrombus to form a new pseudo-intima, the remaining yellow area could appear like a "subintimal plaque." The pericardium itself did not appear to be involved in the process. No evidence of calcification or ossification was observed.

The discolored area and host aorta, for control, were studied by the following methods: (1) for cholesterol and its esters by Schultz's method[7]; (2) for lipid by a modified oil red 0 stain[8]; (3) for hemosiderin (iron) by Gömöri's modified method.[7] As a result of these histochemical tests and stains, it was found that the yellow and orange colors were the result of a variable accumulation of cholesterol, lipid, and hemosiderin. They were concentrated in the mural thrombus and adjacent pseudo-intima but apparently not in the pericardium. By comparison, these substances were not found in the normal aorta. The lipid was distributed in the form of minute droplets with no appreciable evidence of acicular slits or lipoid granulomatous reaction. The lipid sometimes became more condensed within a fibrous connective tissue base in the deeper, more organized layers of the thrombi. Hemosiderin and related hemoglobin pigments tended to be distributed at random throughout the organizing thrombus. It was postulated that the cholesterol and lipid were derived from the blood stream and the hemosiderin from the breakdown of erythrocytes.

Considerable individual variations in blood element deposition and mural thrombosis were present and must have been related to such factors as improper tension on the graft causing surface irregularities and various luminal

disproportions between graft and aorta. Inherent deficiencies in the pericardial surface may have been a factor, but these same surface phenomena have been observed by the author in nylon *cloth* grafts alone. The high blood pressure, large cross section, and rapid turbulent flow peculiar to the thoracic aorta must have been of some importance in the pathogenesis of these phenomena. In the absence of gross errors in surgical technique, these grafts did not undergo progressive thrombotic occlusion. Autogenous pericardial grafts in the thoracic aorta of the dog have been shown to remain patent on aortography as long as three years.[5] Careful histopathologic study of long-term pericardial grafts will be necessary for complete evaluation of the method.

SUMMARY

1. Aortic grafts fashioned from autogenous pericardium, nylon net, and a thrombin-fibrinogen coagulum appeared to function satisfactorily for periods up to slightly less than one year. Long-term follow-up studies will be necessary for complete evaluation of the method.

2. Attention is directed to certain aspects of mural thrombosis and lipid deposition encountered in the grafts.

3. An aortic polythene by-pass shunt and a method of aortography by direct transventricular needle puncture are described.

I wish to acknowledge the help of Captain James Bowman with certain aspects of histopathologic technique.

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DISCUSSION

DR. J. KARL POPPE, Portland, Ore.—I should like to ask Dr. Adler whether heparin dissolves the thrombin and fibrinogen coagulum used to hold together his grafts. My own experience has indicated the necessity for preliminary moistening of the graft with heparin to prevent clotting during its insertion. This seemed particularly true when inserting grafts in the thoracic aorta with a temporary polyethylene tube shunt inside the lumen, permitting a slight but continuous leakage of blood into the graft during its insertion.

Orlon fabric grafts moistened with heparin before use tended to leak unduly and fabric grafts without heparin tended to fill with clots during insertion in the thoracic aortas of 10 dogs

This difficulty was corrected in subsequent dogs by making the fabric impervious to initial leakage by impregnating its outer surface with polyethylene film in an autoclave. The polyethylene filler permitted the use of heparin on the graft with impunity from clotting, leaking, or fraying of the edges. This method differs from that proposed by Shumacker in that only one layer of fabric is used instead of two layers with the polyethylene film between them. Reducing the thickness makes the material more pliable and permits greater ease in turning back the cuffs.

DR. PAUL W. SANGER, Charlotte, N. C.—The search for the ideal substitute for the arterial graft continues. This is because the maintenance of an arterial bank is impossible in many situations and also because the homograft still leaves something to be desired. For these reasons we have turned our attention to synthetic materials. We have used an Orlon knit material which is similar to the material in ladies' hose. We have also used nylon woven material which is similar to the weave used for a shirt. These materials have met certain strict criteria: (1) They can withstand sterilization without loss of properties. (2) These fibers are closely constructed to avoid leakage. (3) The substance is made of a fine filament with a smooth inner surface. (4) The materials are nonirritating when placed in the body and are resistant to breakdown and deterioration. (5) Furthermore, they are strong when wet, and they resist deformity and stretch in the longitudinal plane under conditions contained in the experimental animal and the human body.

They have some disadvantages, however. The synthetic tubes used in the past have had a longitudinal seam, and the material has frayed at the cut edge making it necessary to cuff it for an end-to-end anastomosis with the host vessel. This introduced a technical problem of having to sew through four thicknesses of material where the seam laps were superimposed.

We felt that a seamless tube would be much more desirable. North Carolina State College School of Textiles and Mr. John B. Sidebotham of Philadelphia worked on this problem with us. They devised a method of knitting and weaving a seamless tube for us.

(Slide) Angiocardiogram showing the graft is patent with normal blood flow distally and with only minimal indentation at the suture line.

(Slide) Graft removed six months after its insertion showing complete covering by glistening pseudoendothelium.

(Slide) The walls of the graft are magnified approximately 50 times. Dense collagenous tissue is found extending through the meshes of the fabric.

(Slide) The characteristic appearance of abdominal and common iliac aneurysms. (Courtesy of Drs. Creech, DeBakey, and Cooley.)

(Slide) Knit Orlon graft in position after removal of the aneurysm. (Courtesy of Drs. Creech, DeBakey, and Cooley.)

We have used this fabric as sleeve grafts in the thoracic and abdominal aortas of 59 dogs, and we and others have also used it in 23 human beings.

The strength of an artery depends upon its elastic tissue. In homografts, the elastic tissue eventually disappears, while in these plastic grafts, the artificial fiber remains intact. Thus, this synthetic fiber seemingly serves as elastic tissue.

This is a material which is cheap, is easily cared for, and can be made available to any doctor.

DR. RALPH DETERLING, JR., New York, N. Y.—In about 1948, we began to implant aortic homografts into the aortas of dogs and, after three years, we were distressed to find calcification, spotty deterioration of the elastic framework, and thinning of functioning grafts. Although we did not encounter aneurysm formation in dogs studied for over five years, these degenerative changes appeared to be progressive. Approximately three years ago, Dr. Lester Vargas and I began to use the tulle-weave nylon referred to in this paper, having selected it because of the wide interspaces, elasticity, and strength. It was used as external support to arterial, venous, and pericardial grafts in dogs, so as to restrict tendency to dilatation of these grafts. When we reported this work one year after its inception, we were quite delighted with the results.

(Slide) On the left is an aortogram which shows a graft of the external jugular vein in the thoracic aorta of a dog at about one year. There is elongation and aneurysmal dilatation of the implant. On the right is a similar graft supoprted by the tulle net for one year, and there is no significant change from the time of implantation.

We have now followed these dogs for over three years and I must rise to state that 3 of about 15 have shown significant late dilatation despite external support by nylon net. A careful dissection of these grafts, which were autogenous inferior vena cava implanted in the thoracic aorta, revealed rupture of the nylon strands at the loops of the tulle weave. This weave has a knotting of each fiber as it crosses another, in contrast to a taffeta weave, for example. This knotting would be an advantage, we thought, in preventing slipping of the threads and in imparting maximal elasticity to the net. It appears, however, that the nylon fiber "fatigued" at the knot with continuous pulsatile stress, and eventually broke. It is significant that it was not until after two and a half years that we saw this, and emphasizes our contention that long-term follow-up is essential in vessel replacement programs.

We supported aortic homografts in about 12 clinical cases but, fortunately, because of the size of the vessel, I generally used three or more layers of the net about the grafts. In one patient with a single layer about an aneurysm which could not be removed because of renal arterial involvement, there was subsequent increase in size of the aortic aneurysm. The patient died of rupture of the aorta well above the net, about sixteen months later.

With regard to the use of synthetic materials for blood vessel replacement, we have had extensive experience at Presbyterian Hospital. Following the pioneer work of Dr. Blakemore's associates, my own laboratory group have joined forces in evaluating the various materials suitable for use as grafts. Accordingly, over 130 dogs have been studied for up to four years. There have been about 70 clinical replacements of aorta or peripheral arteries during the past two years by Drs. Blakemore, McAllister, and myself. A taffeta weave of Vinyon-N, nylon, or Dacron has been employed, with very satisfactory results. I must express a word of caution, however. The ready accessibility of synthetic fibric from casual sources has encouraged surgeons to use these materials for vessel replacement, often with no technical information about the material and, unfortunately, at times without adequate technical background. These fabrics should be obtained from reliable sources and have been well tested before clinical use. Certain textiles used for clothing have dyes, toxic additives, and roughening processes employed in the finishing, that might make them unsafe for medical use. The braided tubes are promising, but have not had an extensive nor long trial as vascular replacements. For any of these synthetic materials to have good function, they must be used in the proper cases, and must be implanted with meticulous care.

DR. RICHARD H. ADLER, Denver, Colo.—In answer to Dr. Poppe's question, we have not found it necessary to use heparin postoperatively because the grafts have all remained patent. Mural thrombi were found at post-mortem examination of some grafts but these did not appear to progress and cause occlusion of the lumen. The few grafts that had evidence of thrombi extending further were due to technical errors at the anastomoses. Along this line, I should like to mention another material we are also using by itself, which is a type of "calendered" nylon cloth. As I understand this process of heat pressing, the microscopically demonstrable spaces between the fibers become relatively diminished. I hesitate to mention this because the encouraging course of these grafts is only a little over six months old. In dogs, we have replaced the entire descending thoracic aorta and are making aortic arches with satisfactory results. Blood is let back into the graft which is surrounded by surgical sponges and manual pressure is exerted to counteract the blood pressure. After one to three minutes, the sponges are removed and no bleeding occurs. As a result, we have not found it necessary to use a method of thrombin coating or polythene sheet with this calendered nylon fabric to control leakage. We have successfully used this material in one human patient to replace the aorta from below the renal arteries to both external iliacs. I was interested in hearing Dr. Deterling's comments about the two- and three-year follow-up, and that again emphasizes the importance of long-time follow-up on these types of plastic materials before one can draw definite conclusions.

THE LYMPHATIC DRAINAGE OF SILVER-COATED RADIOACTIVE GOLD COLLOID FOLLOWING INTRATHORACIC ADMINISTRATION TO PNEUMONECTOMIZED DOGS

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NASHVILLE, TENN.

THERE is no need to dwell upon the morbid statistics of bronchogenic carcinoma. In an attempt to improve the results currently obtained by surgical and radiologic methods, investigation of the therapeutic value of radioactive isotopes has been carried out at the Nashville Veterans Administration Hospital. Our interest was drawn to Au^{198} for 85 to 90 per cent of its energy is emitted as beta particles with a penetration of 0.3 mm. (water) and thus evidence radiologic selectivity.

Radioactive Au^{198} administered intrabronchially has been found in the regional mediastinal lymph nodes, as has been previously reported from this laboratory.[1] Unfortunately, Au^{198}, with a half-life of 2.7 days, moves slowly from its point of application, and its energy has been largely expended by the time it appears in the regional lymph nodes.

Hahn[2] has shown that radioactive colloidal Au^{198} treated with silver nitrate and ascorbic acid resulted in a preparation which retained the characteristics of gold from a radiologic standpoint but behaved as a silver colloid in the tissues, with rapid absorption into the regional lymphatics and lymph nodes. Hahn and Carothers[3] have shown that the intrabronchial administration of this silver-coated gold results in an early appearance of the colloidal material in the mediastinal lymph nodes in a significant quantity.

This paper reports the results of silver-coated gold introduced into the empty hemithorax of dogs following pneumonectomy.

Mongrel dogs, 10.5 to 19.5 kilograms in weight, were subjected to pneumonectomy. At various times during the postoperative period silver-coated gold colloid was injected into the empty hemithorax, the dosage ranging from 11 to 150 mc. The dogs were sacrificed at various intervals postinjection, ranging from two to forty-four days. There was one death in this series, Dog No. 18 died on the thirty-first day after injection from pneumonia, which was felt to be unrelated to the therapy.

At autopsy, representative lymph nodes were dissected out, cleansed of adventitial tissue, weighed, placed in formaldehyde, and the radioactivity deter-

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mined in a Texas well counter. Histologic studies were done. The following nodes were studied: right bronchial, carinal, left bronchial, anterior superior mediastinal, right superior mediastinal, left superior mediastinal, right supraclavicular and left supraclavicular. These are illustrated in Fig. 1.

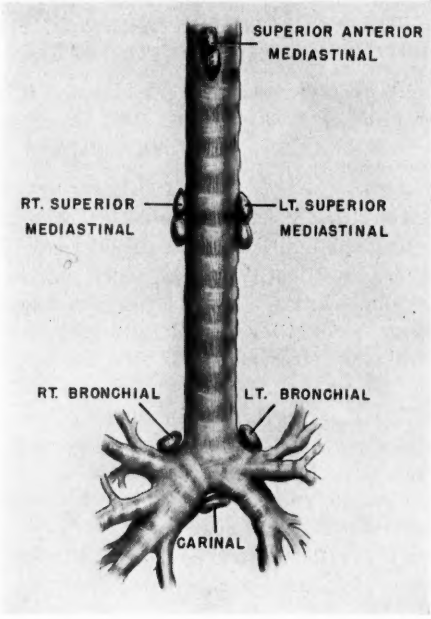

Fig. 1.

In addition, specimens of the parietal pleura, the pericardium, the liver, and spleen were studied. Gross inspection of the hemithorax at autopsy showed no evidence of inflammation. Bronchial stumps healed well in all cases. Histologic study of the liver, spleen, and, in 1 case, the bone marrow showed no abnormalities.

RESULTS

Significant quantities of the colloid material were found in the mediastinal nodes in dogs sacrificed on the second day. Dogs sacrificed later did not have significantly more gold in the nodes studied. In calculating the beta equivalent roentgens, only the radiation emitted after forty-eight hours was determined. In all dogs studied, the mediastinal nodes received the greatest amount of irradiation; only a rare hilar node received significant amounts. The length of time between operation and injection of the isotope did not seem to alter the results. For convenience the dogs can be divided into two groups.

Group I consists of dogs that received a dose of 40 mc. or more. There were 10 dogs in this group (Table I). It will be noted that in this group the anterior

superior mediastinal nodes received adequate irradiation in all instances and the right superior mediastinal and left superior mediastinal nodes in about 70 per cent of the cases. In Dogs No. 18 and No. 19 a long interval existed between injection and counting. Counts on these dogs, due to the rapid decay curve of gold, were too near the background count to permit calculation of the radiologic effect. However, histologic studies showed these nodes to be markedly disorganized. If these are considered as having received adequate irradiation, the percentage is then 90 per cent.

TABLE I. GROUP I, DOGS RECEIVING 40 MC. OR MORE

NUMBER	DOSAGE	β SUPERIOR ANTERIOR MEDIASTINAL	β SUPERIOR MEDIASTINAL LEFT	β SUPERIOR MEDIASTINAL RIGHT
26	44.4 mc.	28,546	5,855	13,270
27	44.4 mc.	199,254	181,032	315,675
14	50.0 mc.	6,211	96	85
12	50.9 mc.	88,632	3,451	2,096
8	52.0 mc.	198,077	9,869	48,735
9	52.0 mc.	83,220	52,440	96,777
10	52.0 mc.	34,940	16,783	Lost
18	75.0 mc.	150,314	Count too near background	Count too near background
19	75.0 mc.	365,489	Count too near background	Count too near background
28	150.0 mc.	94,620	86,549	181,716

Group II consists of 11 dogs that received less than 40 mc. (Table II). This table shows the beta equivalent roentgens received in the three groups of mediastinal lymph nodes in these dogs. With this smaller dosage, results were less predictable. Even with these doses the anterior superior mediastinal nodes received therapeutic irradiation in about 40 per cent of the cases.

TABLE II. GROUP II, DOGS RECEIVING LESS THAN 40 MC.

NUMBER	DOSAGE	β SUPERIOR ANTERIOR MEDIASTINAL	β SUPERIOR MEDIASTINAL LEFT	β SUPERIOR MEDIASTINAL RIGHT
4	11.0 mc.	1.7	14,963	3
5	11.0 mc.	3,419	2,637	27
6	11.0 mc.	8,245	Lost	4,120
29	12.0 mc.	Lost	19,228	2,518
24	13.6 mc.	147	6,474	2,598
25	13.6 mc.	3,878	11,509	6,236
32	15.0 mc.	31,372	1,294	711
33	15.0 mc.	78,295	746	149
35	15.0 mc.	184,244	59	413
15	32.0 mc.	2,757	100	770
16	32.0 mc.	2,766	20,200	10,200

Microscopic study of the mediastinal nodes showed destructive changes which were roughly, but not constantly, proportional to dosage and elapsed time. In the most severe form, there was total necrosis of the nodes and the immediately surrounding tissues, including blood vessels large enough so that the smooth muscular layer could be identified (Fig. 2). In the less severe forms, the nodal architecture was partially preserved, but there was more or less complete loss of lymphocytes; plasma cells and reticulum cells were prominent

survivors in these nodes (Fig. 3). Evidence of regeneration of lymphoid tissue was observed in some long-term survivors. Erythrophagocytosis was a prominent feature in nodes with high counts from animals sacrificed early and also in some with moderately high counts sacrificed later.

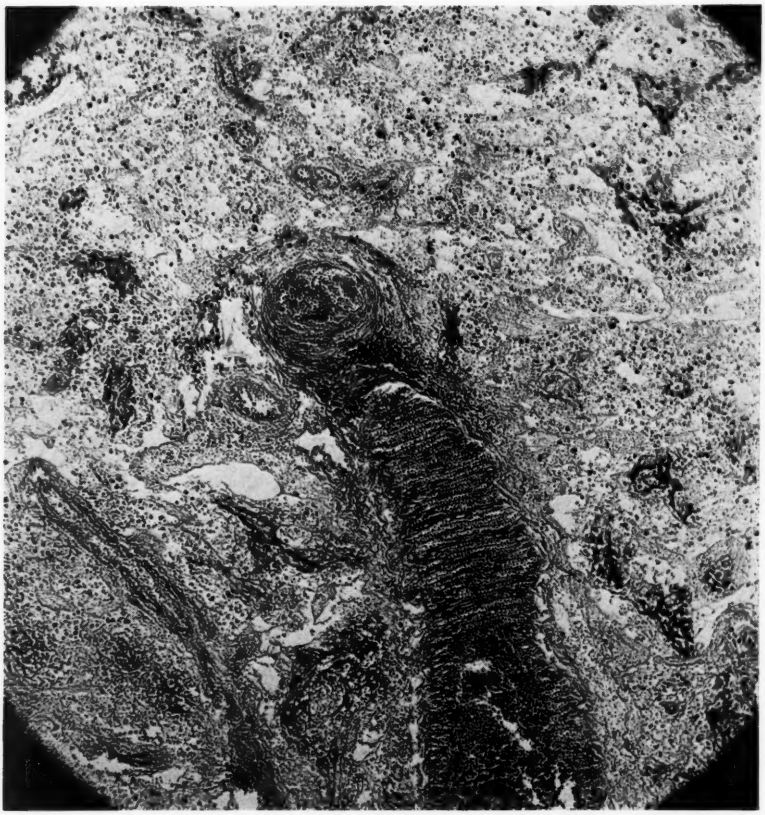

Fig. 2.

DISCUSSION

One can conclude from this experiment that the parietal and mediastinal pleurae in pneumonectomized dogs drain into the mediastinal nodes and that in normal dogs these nodes may be destroyed by the intrapleural injection of radioactive silver-coated gold colloid solution.

It is unlikely that lymph nodes replaced by tumor would pick up sufficient radioactive material to sterilize them. It is not unreasonable, however, to believe that small emboli in these lymph nodes could be destroyed by this method. One of the great advantages of this form of treatment is the easy manner with which it may be used as an adjunct to surgery.

If these observations prove to be valid in the human being, a prophylactic type of mediastinal dissection could be added to pneumonectomy in the treatment of patients with resectible bronchogenic carcinoma.

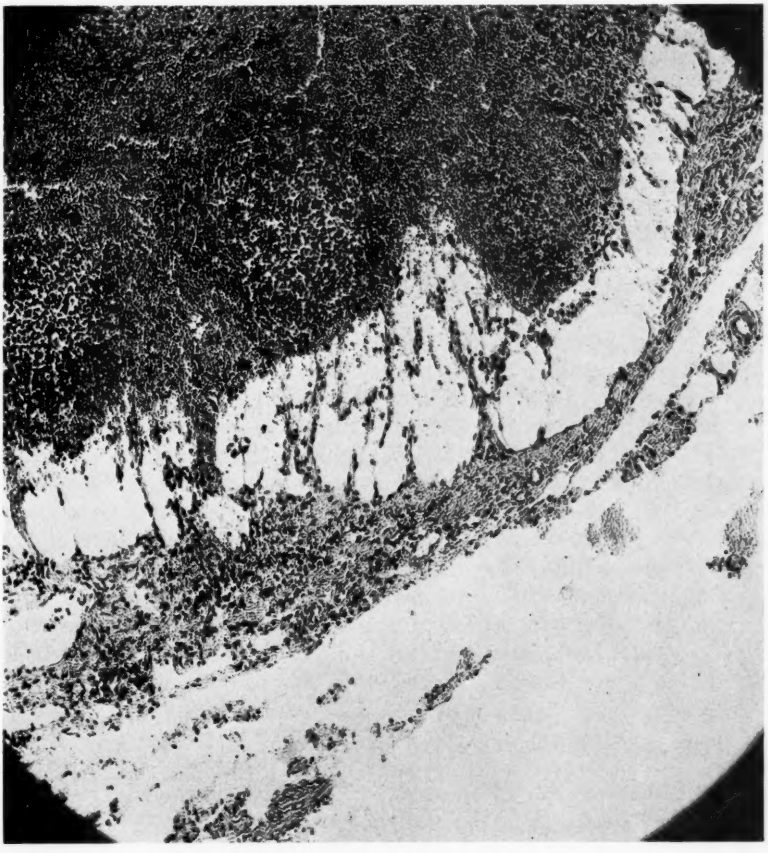

Fig. 3.

Currently at the Nashville Veterans Administration Hospital, silver-coated radioactive gold colloid is being injected into the empty hemithorax of patients who have had pneumonectomy for bronchogenic carcinoma. The dosage has ranged from 75 to 150 mc. It is much too early to analyze the results of this procedure; however, to date no ill effects have been observed.

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Discussion

DR. REX PERKINS, Birmingham, Ala.—We have done animal work of a similar nature, and our findings agree with those that Dr. Carlson has so well presented. The bronchial stump healed well in the presence of heavy doses of radioactive Au^{198} despite the fact that we encouraged disruption by leaving the stump long, using heavy silk, and not pleuralizing the stump. The gold is taken up by hilar and mediastinal nodes, as demonstrated by tissue count and radioautographs. We were unable to correlate closely the size and duration of dose with tissue counts and radioautograph picture. We are at present continuing this work in an effort to quantitate nodal uptake more closely.

As we know, certain dyes injected near a cancer tend, by lymphatic spread, to circumvent the cancerous nodes and go to normal nodes. This may also happen in the situation we are considering with Au^{198}. Nevertheless, since the procedure is safe, and since the Au^{198} is taken up by mediastinal nodes, including those of the opposite side, in quantity sufficient to destroy the nodes, we feel that this procedure deserves an extensive controlled clinical application.

CIRCUMFERENTIAL SUTURE OF THE MITRAL RING

A Method for the Surgical Correction of Mitral Insufficiency

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Philadelphia, Pa.

THE concept for reducing the size of the annulus in valvular insufficiencies as a method for the correction of this dysfunction has been presented in previous publications.[1, 2] Compared to the principle of replacement of occluding valvular elements, upon which practically all previously suggested techniques are based,[3-12] the reduction of the valvular ring by circumferential suture has several theoretical and practical advantages. This is especially true when applied to the atrioventricular valves, more specifically the mitral valve. These advantages include the fact that this procedure does not require the introduction of foreign materials across the lumen of the cardiac chambers. It makes full use of all remaining valvular substance capable of function. The effective orifice of the atrioventricular communication is not encroached upon by plugs or sutured cusps. It involves no more intracardiac manipulation than does a commissurotomy and results in no significant myocardial trauma. It not only makes possible the elimination or reduction of regurgitation, as will be shown, but it is plausible to expect that the size of the atrioventricular ring will be rendered incapable of progressive enlargement. This principle, with or without concomitant commissurotomy, appears applicable to most forms of mitral insufficiency.

Three of the foregoing statements merit further clarification. Techniques involving the use of prosthetic plugs or leaflet suturing methods are associated with considerable operative trauma and with unavoidable reduction in the capacity of the effective valvular orifice. The placement of any known material across the lumen of the vascular chambers has long been known to result in a very high incidence of thrombosis frequently giving rise to embolization. Tissue grafts which are subjected to the pressures extant in the heart chambers (particularly the ventricles) will initially swell and present a serious danger of obstruction. These tissues ultimately fibrose and shrink, completely losing their flexibility.[13-15] A surgical procedure which can achieve the desired result

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without the use of intracardiac foreign materials and without impeding blood flow would seem to be, physiologically and anatomically, a more acceptable approach to the problem of mitral regurgitation. In a sense, the circumferential suture procedure can be compared to techniques used in stenotic valvular disease in which the success attained is, in great measure, due to the fact that these techniques necessitate intracardiac manipulation only and do not otherwise alter the structures involved.

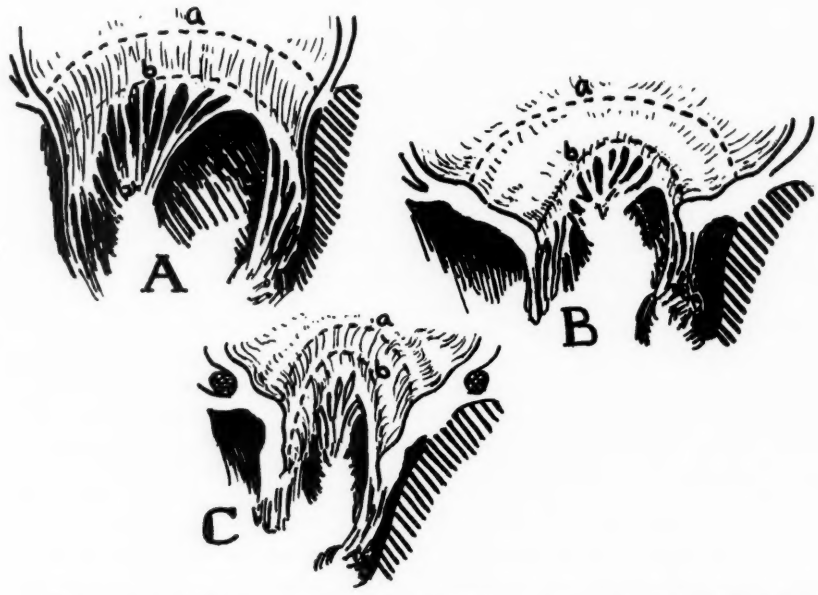

Fig. 1.—A semidiagrammatic representation of the: *A,* Normal mitral valve ring and leaflets in diastole.

B, Diseased mitral valve in which marked insufficiency with enlargement of the ring is present. This figure attempts to show the discrepancy between the "potential" (a) and "effective" (b) orifices.

C, Represents the circumferentially constricted A-V ring illustrating the relaxation of the leaflets and the freedom of the effective orifice. (See text.)

The anatomy of the mitral valve utilizes the basic construction principles of simple, unidirectional mechanical valves. The flow through such valves depends upon the size of the orifice opened when the occluding elements retract. This can be termed the *effective orifice.* The efficiency of the valve depends not only on its ability to open and provide minimum resistance to diastolic flow but also on its capacity completely to occlude the communication between the chambers involved during systole. This communication can be termed the *potential orifice* because it is that which would result if one were to remove or destroy all valvular substance. In the normal mitral valve (as well as in the tricuspid), the retractility of the leaflets provides an opening (the effective orifice) which almost equals in total area that encompassed by the annulus and ventricular inflow tract (the potential orifice). In the diseased valve, however, commissural fusion, leaflet

thickening and rigidity, shortening of chordae tendineae, and enlargement of the annulus, all tend to increase the discrepancy between the effective and potential orifices. Circumferential suture of the regurgitant atrioventricular valves is logical because reduction of the area of the potential orifice can thereby be accomplished without significant encroachment upon the effective orifice. This is so because of the pathologic morphology of the valve, as there is usually a substantial amount of potentially functional valvular tissue between the two orifices (Fig. 1).

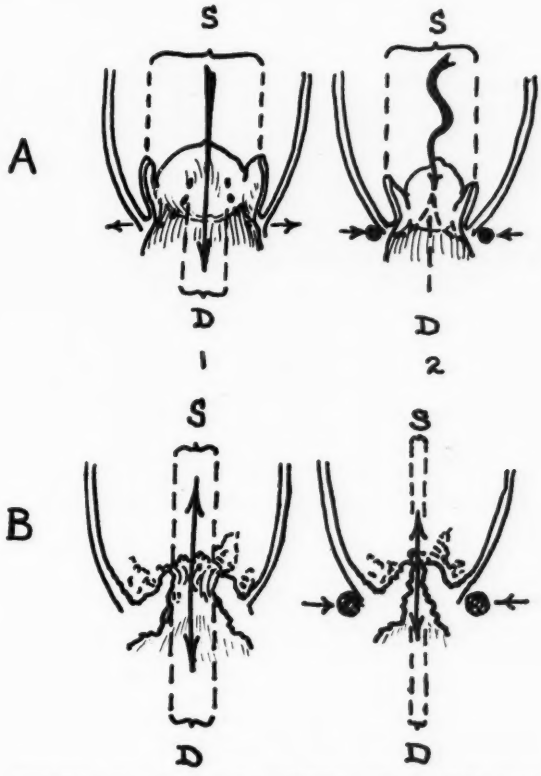

Fig. 2.—*A*, Illustrates the situation in syphilitic aortic insufficiency where a dilatation of the valvular ring plays a prominent role (1). Conceivably, constriction of the annulus (2) could eliminate insufficiency without producing stenosis because the cusps remain pliable and are able to function reasonably well.

B, Represents the contrasting situation in nonsyphilitic aortic valve disease where the insufficiency is associated with fixed, rigid cusps incapable of motion (1). Constriction of such a valve ring (2) would seem to be inevitably associated with an aggravation of stenosis in inverse proportion to the relief of insufficiency. (S: systole; D: diastole.)

In certain types of regurgitation of the ventricular outflow valves (i.e., syphilitic aortic and relative pulmonic insufficiencies), it is quite conceivable that circumferential constriction may reduce the discrepancy between the corresponding effective and potential orifices without significantly embarrassing forward flow. On the other hand, in those conditions in which aortic insufficiency is

associated with extensive scarring, calcification and fixation of the cusps, it appears doubtful that the principle of annular constriction can be applied for the reduction of regurgitation without producing serious degrees of stenosis. This is true because pathologically there is a rigid continuity of the cusps with the ring upon which they are supported (Fig. 2). In such cases, there is not the residual pliability that one finds in the diseased mitral valve.

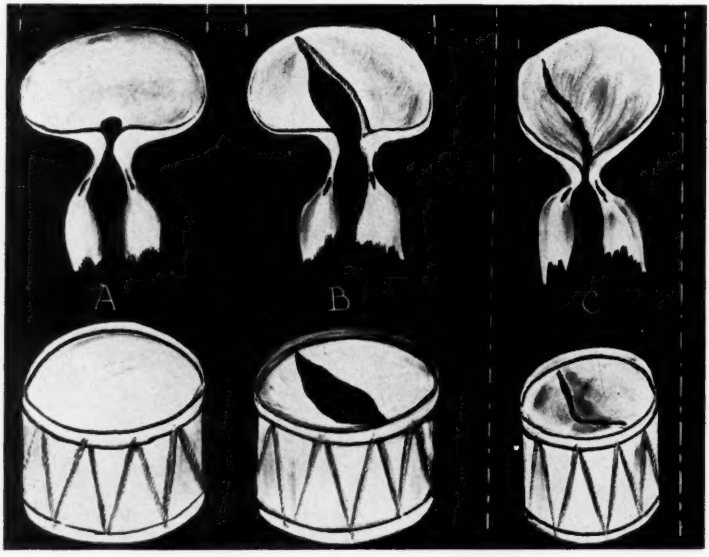

Fig. 3.—*A*, In a diseased mitral valve which is both stenotic and insufficient the leaflets are under tension in a manner similar to a stretched drumskin.

B, If a commissourotomy is performed, stenosis should be relieved, but serious regurgitation frequently results as a consequence of the separation of the cusps. This is comparable to the gap which results if one slashes a taut drumskin.

C, If the annulus is reduced in size the leaflets can relax and can be enabled to come in contact with each other. This is comparable to mounting the slashed drumskin from a large drum on one of smaller diameter.

It has been noted that in a large number of mitral valves in which there is a combination of stenosis and insufficiency there is, also, a significant degree of annular dilatation which places the leaflets under severe tension and further hampers their ability to move (Fig. 3). Edwards[16] has described a phenomenon comparable to a sliding herniation in which the annulus is displaced upward (toward the atrium) in cases of severe mitral insufficiency.

It should be understood, then, that the efficacy of the procedure herein presented depends directly upon the degree of valvular mobility or residual potential function found in any given instance. Its mechanical limitations, therefore, appear to be similar to those of mitral commissurotomy. If one should be confronted with an incompetent but solidly calcified, rigid, unyielding valve, such as those which, when stenotic, respond but poorly to commissurotomy, the result of circumferential suture might likewise be unsatisfactory. Fortunately,

such cases are in the minority. In such situations, nothing short of actual valve replacement will suffice. Until such a feat is possible, however, in serious degrees of surgically produced or existing insufficiency in association with such a valve, one may speculate that placement of a circumferential suture might be of value if only to fix or stabilize the size of the ring, even though the initial degree of regurgitation be but slightly reduced or remain unchanged.

Based on the arguments just presented and after a study of the pertinent anatomic features in normal and diseased human valves, an experimental program was initiated to investigate the problems associated with the correction of valvular insufficiencies by the circumferential constriction of the annulus. To date, this work has involved experimentation on some 150 dogs. In the course of these studies, a well-grounded technique for the correction of mitral insufficiency has been evolved. This communication deals with the study of 80 animals in which this procedure was performed. The technique as used here is the result of modifications of various approaches tried in preliminary experiments. The results of the initial clinical trials are also included.

EXPERIMENTAL WORK

In a series of eighteen acute experiments,[17, 18] mitral insufficiency was produced by either tying the mural (posterior) leaflet to the heart wall or by lacerating this leaflet with a hooked knife. The resulting regurgitation was then corrected by placing a circumferential suture around the annulus. In every case, an excellent regurgitant jet was palpable to the intra-atrial finger. A gross thrill was evident on the surface of the atrium, and the typical changes of insufficiency were recorded in pressure pulse tracings. In each instance, the regurgitation was either completely eliminated or reduced to practically undetectable degrees (Figs. 4 and 5). To accomplish this, it was necessary to constrict the mitral ring to a diameter which was never less than 2.3 cm. (4.1 sq. cm.) in the 9 dogs in which regurgitation was produced by tying the leaflet. The diameter of the constricted ring in 8 of the 9 dogs in which the cusp was lacerated was never less than 1.8 cm. (2.5 sq. cm.). In the ninth animal, constriction had to be carried to a ring diameter of 1.4 cm. (1.5 sq. cm.). These subjects were sacrificed in order to check the placement of the suture and to determine the extent of valvular immobilization or laceration as well as the degree of constriction.

A study of the circumferential suture technique and its possible consequences was carried out in a separate series of 62 dogs ranging in size from 25 to 60 pounds. These healthy, adult mongrel dogs were anesthetized with pentobarital sodium (15 to 30 mg. per kilogram of weight) and ventilated by connecting a Pneophore* or a homemade circular-valve type of respirator to a rigid endotracheal cannula equipped with a pneumatic cuff. Electrocardiograms were made on the anesthetized animals before surgery, recording the standard and unipolar limb leads as well as the usual six chest leads. In the first 28 animals a "clean" technique was followed. In the remainder, strict asepsis was observed.

*Mine Safety Appliance Co., Pittsburgh, Pa.

Technique.—The left chest was entered through the sixth interspace and the pericardium opened after mobilizing the phrenic nerve. A hemostatic purse-string suture was placed about the base of the left atrial appendage. Pressure tracings were then taken singly in the left atrium, left ventricle, aorta, and pulmonary artery. The circumferential suture was placed and the series of tracings was repeated before tying the suture, five minutes after it was tied to

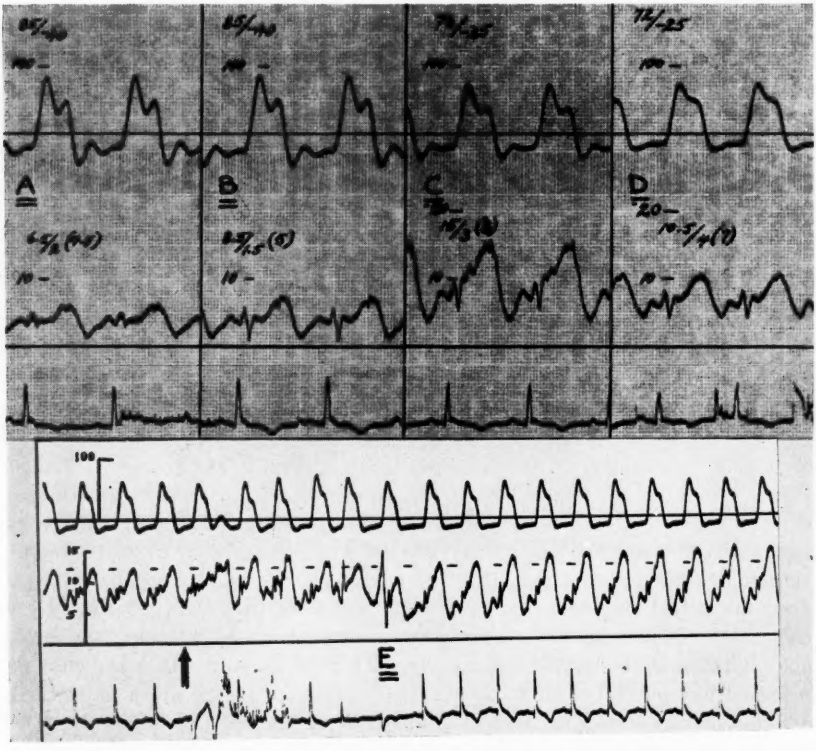

Fig. 4.—*A,* Pressure tracings taken in a dog after exposure of the heart. *B,* After placement, but before tying the circumferential suture the same tracings were taken. *C,* This was repeated after production of mitral regurgitation by lacerating the mural leaflet. *D,* Tracing taken after tying of the suture to a ring diameter of 1.8 cm.

Upper tracing: left ventricle, middle: left atrium, lower: ECG Lead II. Note the reversal of both pressure and contour of the tracings after the suture was tied.

E, Same experiment. To the left of the arrow is the tracing obtained after correction of the regurgitation. While a continuous recording was made, the circumferential suture was cut and pulled out (at arrow). Note that after this point the regurgitant contour and pressure changes reappear.

1.8 to 2.0 cm. in diameter, and again twenty minutes after tying the suture. The measurement of the constriction was determined by measuring the operator's left index finger and constricting the ring around a predetermined point on this finger. The pericardium was closed in all animals in which no pericardial bolster was used (described later) and left open in the others. The lungs were inflated and the chest was closed with wire. The electrocardiogram

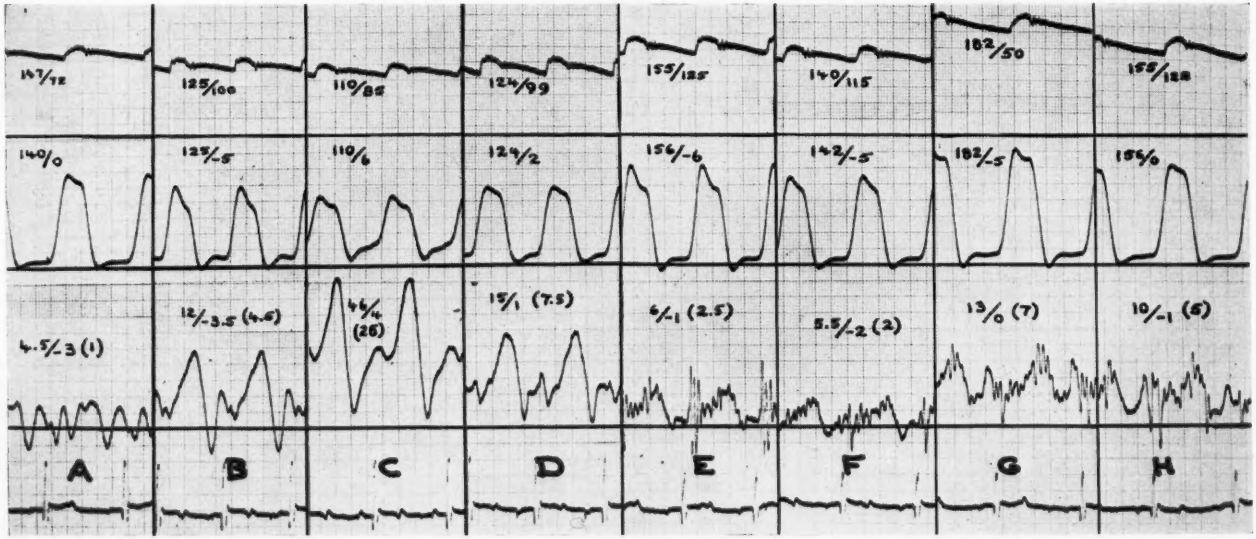

Fig. 5.—An experiment in which: *A*, An initial set of pressure pulses was recorded. From above downward are the aortic, left ventricular, left atrial, and ECG Lead II tracings. *B*, Mitral regurgitation was produced by lacerating the mural leaflet. *C*, Methoxamine (0.5 mg.) given intra-arterially. Note the enormous rise in left atrial pressure and the exaggeration of the regurgitant contour. Note also the failure of the left ventricular and aortic pressures to rise. *D*, Ten minutes after the administration of Methoxamine the left atrial pressure drops to a level close to that seen in *B*. *E*, The circumferential suture was now tied to 2.0 cm. Note the immediate changes in pressure and contour. Note also the increased amplitude of the vibrations of valvular closure (c wave) in the left atrial record. The aortic and left ventricular pressures rise. *F*, The recording repeated ten minutes after the suture was tied showing a further drop in atrial pressure. *G*, At twenty minutes after the initial dose of Methoxamine (*C*) a second equal dose was given, but now the circumferential suture had been tied. Note the marked rise in ventricular and aortic pressures but the relatively little elevation in left atrial pressure as compared with that seen in *C* when the mitral insufficiency was uncorrected. *H*, Ten minutes after *G* the tracings were repeated showing a gradual return to normal pressure levels as the effect of the vasopressor wears off.

was repeated at the completion of the operation. The survivors in this series were reoperated upon at one- to six-month intervals. At that time a preoperative electrocardiogram was again made, the chest was opened to expose the heart and a series of pressure tracings was made as before. The animals were then sacrificed for examination of the heart, lungs, liver, spleen, and kidneys, routinely, and of the brain when a lesion was suspected. All hearts were preserved in Formalin and paraffin histologic sections made of cuts from selected points on the mitral ring and myocardium as well as of other organs which might have been grossly suspected of pathology.

The suture material used in 21 dogs was No. 2 braided silk of three different brands.* In 13 animals, braided cotton umbilical tape was used.† In the subsequent 28 animals, the same cotton tape was placed but in addition a segment of it was covered with a sleeve or bolster of pericardium.

In the first 34 animals, the technique consisted of placing the suture medially by starting for the posterior aspect of the heart at a point just to the left of the posterior descending coronary artery and immediately beneath the coronary sinus and distal circumflex coronary artery. The needle (a large Reverdin, after trial of several types, proved to be preferable) was passed ventrad in the base of the interatrial septum, emerging in the transverse sinus at the junction of the anterior atrial walls with the septum. The posterior tail of the suture was then threaded on a large, curved needle (Mayo or Ferguson type) and stitched anterolaterally into the atrioventricular groove, underpassing the lateral branches of the circumflex coronary so that it finally lay just beneath the circumflex bundle. The anterior tail of the suture was then stitched beneath the circumflex coronary artery and great cardiac vein at a point about 5 to 10 mm. from the take-off of the anterior descending coronary. The two tails were thus brought together a few millimeters to the left of the anterior descending coronary and immediately below the circumflex coronary in the periannular fat pad. At this point they were tied in a double square knot.

In the later 28 animals, the technique was modified in that no attempt was made to keep the medial segment of the suture within the substance of the septum. This portion of the suture was intentionally passed into the right atrium, entering this chamber at a point just ventrad to the ostium of the coronary sinus, then passed adjacent to the right side of the septum, piercing the anterior right atrial wall at its junction with the anterior base of the septum. At this point the suture emerged into the transverse sinus as before. The segment of suture which was to lie in the transverse sinus was then encased in a pericardial sleeve 4 cm. in length. In 8 dogs, this sleeve was left attached as a pedicle graft. In the others, it was detached as a free graft. A tunnel was made anteriorly beneath the circumflex coronary and great cardiac vein at a point about 1 cm. lateral to the anterior descending coronary. This segment of the suture so bolstered was then drawn back into the transverse sinus by traction on the posterior tail. The anterior tail was passed beneath the circumflex through the previously constructed tunnel. In this manner, the

*Davis & Geck: Anacap, Ethicon, and Deknatel black braided silk swaged on 6 inch semimalleable needles made up at our request.

†Gudebrod Brothers braided umbilical tape.

pericardium-covered portion of the suture lay in the groove of the transverse sinus, extending from the anterior walls of the atria, through the tunnel and emerging anteriorly just beneath the circumflex coronary. The posterior tail was next carried anterolaterally, underpassing the coronary branches and tied anteriorly as before (Fig. 6).

The reason for the modifications in the technique used in this last group of dogs, especially the use of pericardial bolsters, was the fact that in two thirds of the animals surviving the placement of either the braided silk or the bare

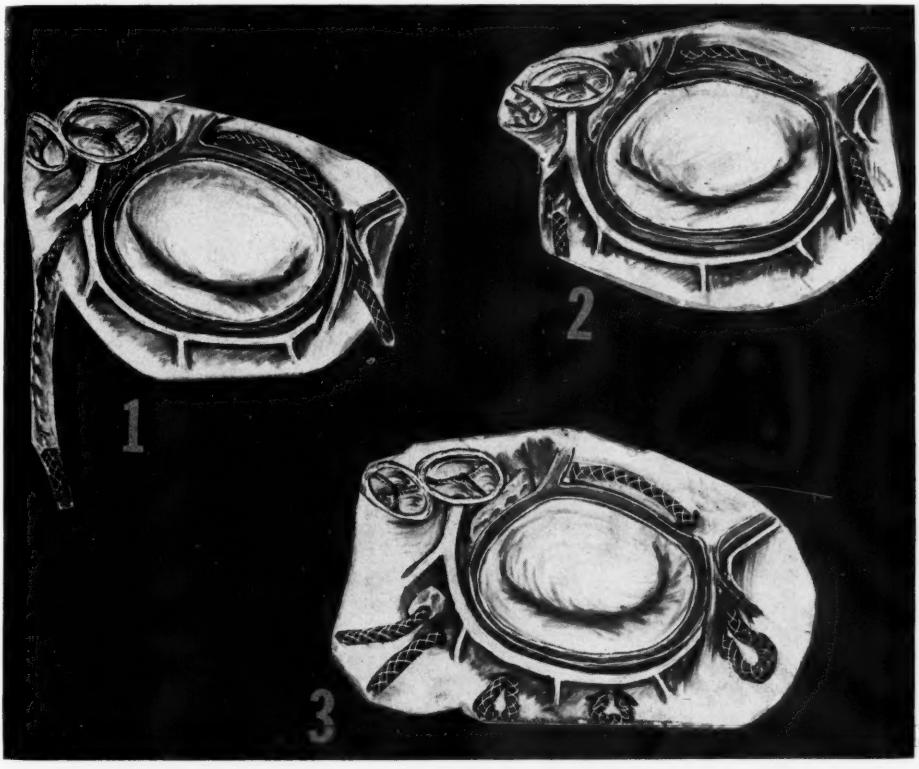

Fig. 6.—1, The medial segment of the circumferential suture placed. A segment of the anterior tail has been wrapped in a pericardial sleeve.
2, The suture has been pulled back, drawing the percardium-covered portion into the transverse sinus. The anterior tail has been passed beneath the circumflex coronary artery through the previously dissected tunnel.
3, The posterior tail has been stitched laterally and anteriorly into the atrioventricular groove to complete the encirclement of the ring.

cotton tape the suture cut through the tissues, eroding into the lumen of the left atrium. It was found that this erosion occurred consistently in precisely the same area, namely, that segment of the ring adjacent to the transverse sinus. The mechanism of this erosion was comparable to that of a string cutting its way through a cake of ice. That is to say, as the suture cut its way inward its

Fig. 7.—*A*, (*1*) Right atrial surface of the interatrial septal base showing the endothelialization and fibrosis which cover the cotton tape (*2*). *3*, Rim of the interventricular septum. *4*, Lumen of the left atrium. (Microphotograph of 1-month specimen. Hematoxylin & eosin, ×10.)

B, Section showing the cotton tape (*1*) buried in the interatrial septum (*2*). *3*, Left atrial lumen. *4*, Interventricular septal rim. The right atrial lumen is on the right side of the illustration. (Microphotograph of 2-month specimen. Hematoxylin & eosin, ×10.)

Fig. 7. (Cont'd).—*C*, The cotton tape was placed into the myocardium where it becomes encased by a fibrous envelope (*1*) and surrounded by healthy heart muscle. *2*, Areolar and fatty tissue of the peri-annular fat pad. (Microphotograph of 5-month specimen. Hematoxylin & eosin, ×10.)

D, Section through the "shelf" taken to show the shelf formation (*1*), the suture (silk) (*2*), the base of the mitral leaflet and (*3*), a portion of ventricular myocardium. (Microphotograph of 6-month specimen. Hematoxylin & eosin, ×10.)

path healed behind it. This resulted in the formation of a curious shelflike projection of fibrous tissue into the lumen of the atrium. This shelf was consistently located a millimeter or two above the valve ring, extending from the anterior limits of the interatrial septum to a point just lateral to the anterolateral commissure, forming a crescent-shaped scar. In most of the specimens, the suture presented in the center of the crescent so that a small portion of it lay exposed to the blood stream. Here, a polyplike mass of granulation tissue, varying in size from 2 mm. to 1 cm. was almost always present (Fig. 7, *A*, *B*, *C*, *D*, and *E*). In 2 animals, erosion was so rapid that an acute, fatal cardiac tamponade resulted.

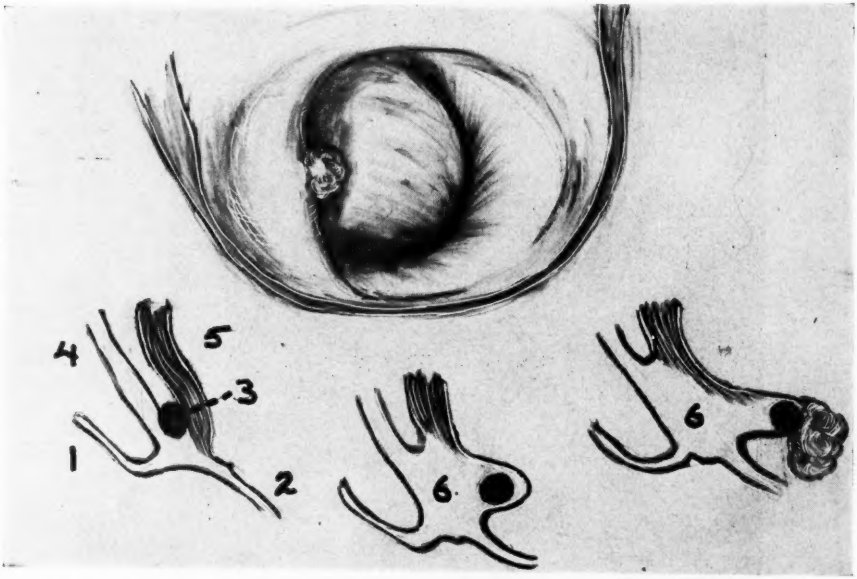

Fig. 7 (Cont'd).—*E*, The diagram at the top of the illustration demonstrates the appearance of the crescent-like scar or "shelf" with its central, "polyplike" mass of granulation tissue, as viewed from the atrial side. Below this diagram are three sections, across the segment of the ring which is adjacent to the transverse sinus, to show the position of the suture in the groove of the sinus and then as it gradually erodes into the atrial lumen. *1*, aortic valve cusp, *2*, mitral valve cusp, *3*, suture, *4*, aortic wall, *5*, atrial wall, *6*, scarring in the path of erosion and obliteration of the transverse sinus groove.

Since the observation was made that the site of erosion was always the same, it was reasoned that this was probably due to the fixation of the annulus at this point to the fibrous framework that supports the tricuspid and aortic rings as well as the mitral, to the thinness of the left atrial wall at the base of the appendage, and to the "sawing" action of the suture. Means for preventing this were considered. Among these, the possible use of other suture materials was prominent. It was thought that a smoother, softer, and larger caliber material might be in order. Tissue strips were thought to be too unreliable since the likelihood of their uncontrollable constricting effect by scarring presented a potential danger of producing too great a narrowing of the ring. While in-

vestigating the possibility of obtaining a more suitable material, it was thought worth while to try covering the offending segment of suture with a pericardial sleeve or bolster. Because of its segmental application, this tissue cover seemed unlikely to produce excessive constriction by scar. At first, this was left attached by a pedicle to the pericardial sac. This resulted in the risk of kinking the circumflex coronary and did not seem to be of any real advantage. The bolster was then made as a free graft, taking precaution to fasten both ends of the sleeve to the cotton tape itself thus preventing "telescoping" of the sleeve on the suture.

Pathology.—None of the specimens in which the suture was prepared with pericardium showed either acute or chronic erosion (Table I).[17] The size of the ring remained essentially the same as that to which it had been tied, except in 2 animals in which at autopsy the ring was thought to have been slightly reduced beyond the original size. The observation period of one to six months in these 62 animals seemed adequate. Note that in 9 of the 18 dogs in which the silk or cotton suture cut through it did so within a month (Table I).

TABLE I. INCIDENCE OF EROSION

SPECIMEN EXAMINED IN		1 WEEK OR LESS	1 WEEK TO 1 MONTH	1 to 2 MONTHS	2 to 3 MONTHS	3 to 6 MONTHS	TOTAL
Silk	Eroded	5	2		1	6	14
	Did not erode	3	1				4
Cotton Tape	Eroded	1	1	1		1	4
	Did not erode				1	2	3
Cotton Tape and Pericardium	Eroded						0
	Did not erode	5	1	1	8	5	20
Criteria for judging erosion were met in							45
Criteria for judging erosion were not met in							17*
				Total			62

*Operative death after suture was placed	7
Operative death before suture was placed	4
Suture transfixing left atrial lumen	
Cotton tape	3
Cotton tape and pericardium	1
Suture not tied	1
Suture could not be placed	1
	17

All varieties of suture were well tolerated by the surrounding tissues. There was a characteristic acute inflammatory reaction around the material, occurring early, which gradually subsided. The cellular infiltration was replaced in a few weeks by a fibrous envelope surrounding the suture. The reaction was somewhat greater around the pericardium-covered segment where scarring occasionally resulted in a fibrous cord of up to 1 cm. thickness. The inflammatory reaction was generally greater in the animals nonaseptically operated upon and was minimal in the aseptically controlled group. In no instance was there histopathologic evidence of damage to the ventricular myocardium as a result of trauma in the placement of the suture when the procedure was performed correctly. Fig. 7 shows some examples of the histologic

features noted. In 4 animals of this series, the suture was placed erroneously within the substance of the myocardium. In these, the material was enveloped by fibrous tissue and surrounded by healthy muscle.

There was some concern as to the fate of the segment of suture exposed to the blood flow within the right atrium. It was thought that this might be a source of thrombo-embolism. It was soon observed, however, that, since the suture lay in contact with the surface of the septum, it was covered by a layer of fibrin and endothelialized within two weeks. There were no instances of thrombosis at this site.

There were a number of technical errors in the performances of the procedure. These can now be avoided if due care is taken during each maneuver. The obvious dangers are related to injury of important coronary branches. Fortunately, these vessels are visible and can be easily by-passed. Transfixion of a segment of the ring by entering the lumen of the left atrium at some point on its circumference is a serious error because this will not only leave a cord of suture across the lumen, which can be the site of thrombosis and origin of

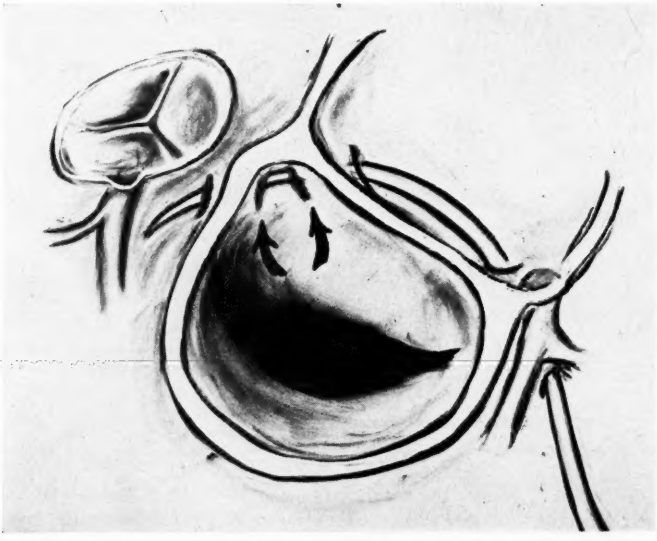

Fig. 8.—This diagram illustrates the tenting of the mitral ring as traction is made on the atrium, to demonstrate the danger of transfixing the atrium at this point. (See text.)

emboli, but also leads to erosion of the tissues by the suture at the points of perforation. The risk of such transfixion is particularly great when attempting to pass from the right atrium into the transverse sinus. At this point, there is a tendency to pull the left atrial appendage with the left hand as the needle is guided with the right. This causes "tenting" of the atrial wall. The apex of this tenting is at a point on the ring just posterior and medial to the anterior commissure and beneath the anterior base of the interatrial septum (Fig. 8).

If one should lose control of the needle at this point there is strong possibility of transfixing this tented segment, crossing the atrial lumen just above the anteromedial commissure. Another danger is the possibility of catching the right wall of the right atrium or the wall of the vena cava if the needle is advanced too far into the right atrium. This was done in 2 animals. In one of these, a definite inferior vena caval obstruction resulted, in the other the error was inconsequential. In 2 animals, the anterior wall of the right atrium, at the point of emergence of the suture, was lacerated seriously. These two errors are easily avoided if the point of the needle is kept close to the septum at all times.

Electrocardiographic and Hemodynamic Studies.—In order to evaluate the suggested operative procedure from the standpoint of possible damage to the heart muscle, the conduction system, the coronary circulation and, also, in regard to potential hemodynamic alterations resulting from decreasing the size of an annulus which was not originally dilated, electrocardiographic, and pressure pulse tracings were used.[18] These studies were done in 62 dogs in which a circumferential suture was placed. The technical modifications which were made from time to time were of such a nature that they could not be expected to affect the outcome in regard to the points just enumerated. Electrocardiograms were made in all the animals immediately preoperatively; postoperatively; at one, two, and six weeks; and again at the time of reoperation one to six months after the initial procedure. These tracings included the standard and unipolar leads as well as the usual six chest leads. In 15 animals, electrocardiographic tracings were also made after each of the important steps during the purse-string suture procedure. In 3 dogs, coronary damage was suspected when they died without apparent cause. The electrocardiogram in these, however, did not confirm this suspicion. The lack of electrocardiographic evidence might have been due to the fact that the dogs died before serial tracings could be obtained. In 2 other animals, a coronary branch was obviously injured at surgery. The injury could have been easily avoided if more caution had been observed. In none of the others was there any definite electrocardiographic evidence of myocardial infarction or of conduction disturbances. There were no arrhythmias except in two animals which showed a transient atrial fibrillation. In 6, the changes noted were compatible with minor degrees of pericarditis attributable to the surgical procedure as a whole rather than to the placement of the circumferential suture itself.

In 15 animals, electrocardiographic tracings were taken during the operation and these were recorded after the following steps: opening of the pericardium; placement of the hemostatic purse-string suture at the base of the left atrial appendage and tunneling of the circumflex coronary artery; placement but before tying of the circumferential suture, and twenty minutes after the suture was tied to 1.8 to 2.0 cm. These tracings indicate that the majority of the changes could be attributed to the thoracotomy and pericardiotomy and were not specifically associated with the placement of the circumferential suture itself.

An analysis of the left ventricular pressure pulse was undertaken as a means for the detection of possible myocardial damage which would not be re-

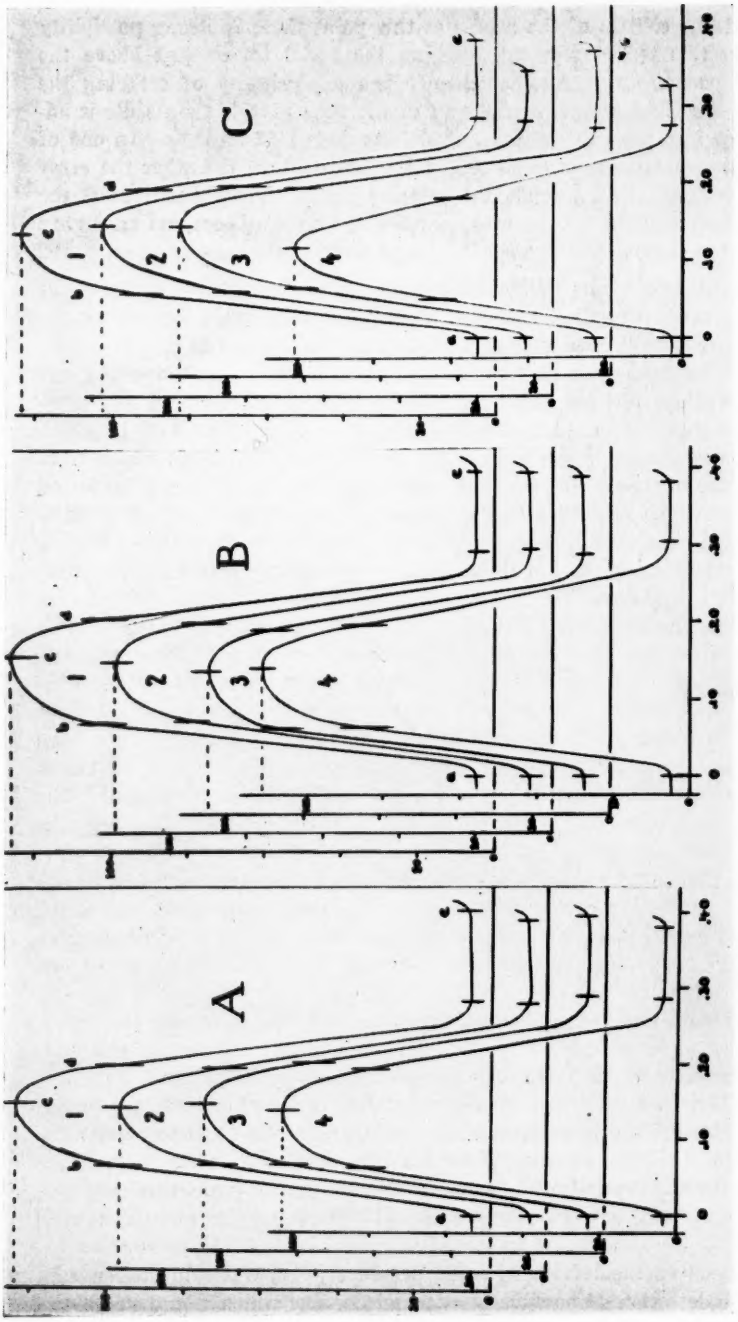

Fig. 9.—Average ventricular pressure curves.
1, Recordings taken initially after exposure of the heart.
2, After placement of the circumferential suture (not tied).
3, Five minutes after the suture was tied.
4, Twenty minutes after the suture was tied. (Plotted in mm. Hg as marked on the left, against seconds as marked at the base.)
A, Average curves in 30 dogs.
B, Average curves in the survivors of those.
C, Average curves in 6 dogs suspected of having had coronary or myocardial damage. (See text.)

vealed by the electrocardiogram. Average ventricular pressure curves were plotted to correspond to each of the following stages of the procedure: initial measurements, measurements with the circumferential suture placed but not tied, five minutes and again twenty minutes after tying the suture. These data are grouped in three categories: (Fig. 9) Group A includes 30 animals thus studied; Group B includes those that survived the operation; Group C includes 6 dogs which died shortly after the procedure, in three of which coronary damage was suspected. A clear-cut cause of death was not found at autopsy in any of these 6 animals. Note that in the first two groups the only significant change in the ventricular curves was a drop in pressure. This can probably be accounted for on the basis of variable degrees of operative blood loss. In Group C, however, the final curve is not only lower but shows a significant alteration in contour. This change is compatible with reduced blood volume but myocardial damage as a result of trauma cannot be excluded.

Both the electrocardiographic and the pressure pulse tracings, then, appear to indicate that although there is most certainly a risk of damaging the coronary circulation and/or the myocardium itself, when the operation is properly and carefully performed there is no evidence of significant damage to either. The total absence of conduction defects was also noted. The 2 animals in which transient auricular fibrillation was seen reverted to normal sinus rhythm by the end of the operation. A myocardial infarct was found at autopsy in only 3 animals of the entire group. In one, a large lateral branch of the circumflex coronary was transfixed with the needle. This accident was obvious at the time of the operation and could have been easily avoided. In the other 2, although the operative technique cannot be held blameless, the infarction could well have been the result of an embolus since there were also multiple infarcts in the kidneys, spleen, and liver. These animals had a circumferential suture of silk which cut through into the left atrial lumen and accounted for the source of emboli.

Pressure measurements were taken in all animals. The studies in 12 dogs which died at operation were incomplete and are excluded from this evaluation. Figs. 10 and 11 show the graphs of the average pressure changes in the left atrium, pulmonary artery, left ventricle, and aorta. There was generally a slight or insignificant elevation in the left atrial pressure. There was usually an insignificant drop in pulmonary artery pressure. There was also a drop of more significant proportions in the left ventricular and aortic pressures. These changes were observed consistently to hold both in the acute and in the long-term studies. It is difficult to attribute the minimal rise in atrial pressure to excessive narrowing of the A-V ring which, even though initially normal, was never reduced to a diameter less than 1.8 cm. (2.5 sq. cm.). The aortic and ventricular pressure drop is probably accounted for by operative blood loss of approximately 150 to 300 c.c. in animals averaging 35 lbs. in weight. In a group of 8 dogs which were supported with either saline-Methoxamine infusion, blood transfusion, or both, the ventricular pressure was higher and the aortic better sustained than in those not supported in this manner (Fig. 11). The fall seen in the measurements taken at reoperation is due to

blood loss again since here none of the animals were supported and blood loss was usually greater due to the need for reincision and reopening of a pleural symphysis usually associated with lung trauma. The elevation in left atrial pressure seen in Group A of Fig. 11 gave us some concern. Since we had noted that in 7 dogs, in which the silk suture had cut through into the lumen, there had been a marked narrowing of the ring to a diameter of about 1 cm., the pressure determinations on these were averaged in order to compare them with the rest (Fig. 12). We were quite surprised to find that there was hardly any elevation in atrial pressure and indeed a slight drop in pulmonary artery pressure. The explanation of the left atrial pressure change, then, cannot really be on the

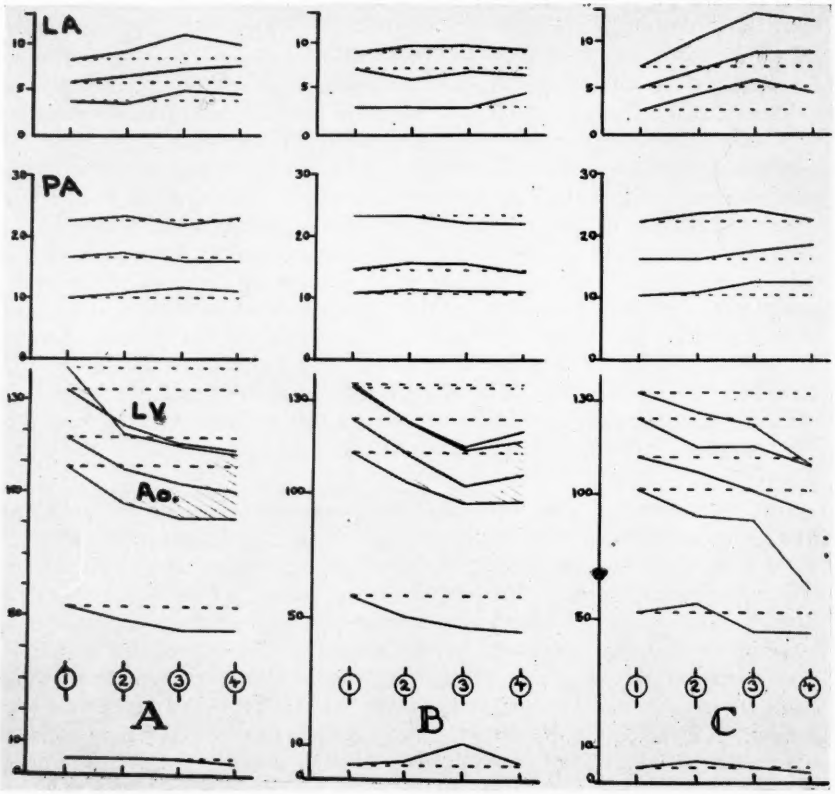

Fig 10.—Average pressures in:
A, Thirty dogs operated upon by this circumferential suture technique.
B, Survivors of this group.
C, Six dogs suspected of having had coronary or myocardial damage. (See text.)
1. Initial pressures.
2. Circumferential suture placed but not tied.
3. Circumferential suture tied for 5 minutes.
4. Twenty minutes after suture was tied.

The upper graphs show atrial pressures. The next, pulmonary artery and the lowest aortic and left ventricular pressures. Maximum, mean, and minimum pressures are charted in each step (mm. Hg).

basis of narrowing of the ring. Perhaps the slight rise in left ventricular diastolic pressure is a clue to circulatory disturbances attributable to minimal degrees of myocardial anoxia resulting from anesthesia or decreased blood volume, or possibly to very minor degrees of transient left ventricular damage which when severe, as in Group C (Fig. 10), might be responsible for the more obvious left atrial pressure rise. As far as the possibility that lowered ventricular and aortic pressures might be masking an otherwise significant elevation in left

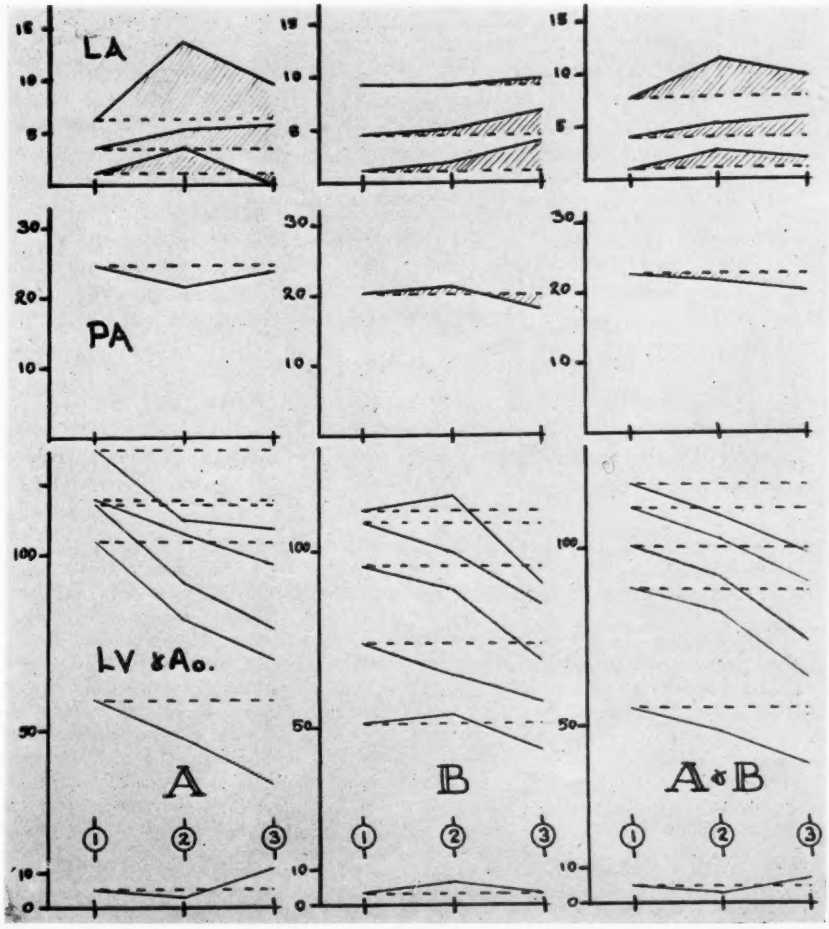

Fig. 11.—Left atrial, pulmonary artery, and left ventricular, and aortic pressures averaged in:

A, Nine dogs in which the circulation was not supported during surgery.
B, Nine dogs in which the circulation was supported with saline-Methoxamine and/or blood infusions during the operation.
C, Average of both groups.
1, Initial measurements, after the heart was exposed.
2, Twenty minutes after the suture was tied.
3, One to six months after the initial procedure.

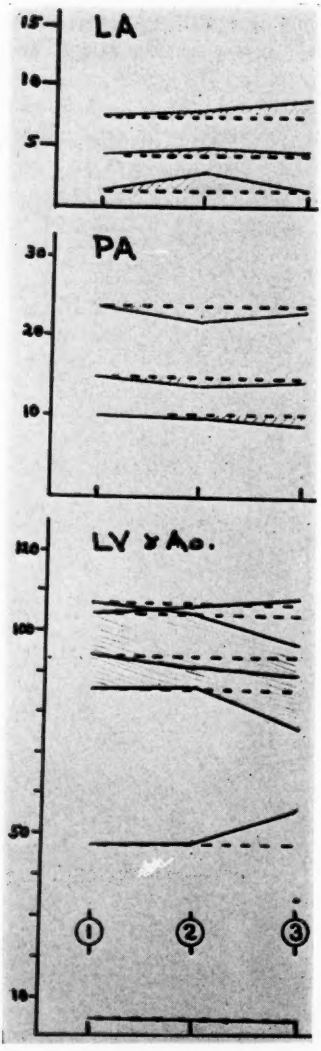

Fig. 12.—Left atrial, pulmonary artery, aortic, and left ventricular maximum, mean, and minimum in 7 dogs in which erosion of the suture had caused scar-contracture of the ring to approximately 1 cm. in diameter.

1, Initial pressures.

2, Twenty minutes after tying the suture to 1.8 to 2.0 cm. in diameter.

3, One to six months postoperatively. (See text.)

atrial and pulmonary pressures is concerned, it is interesting to note that in the dogs which were supported by transfusion or vasopressors and fluid there was no greater magnitude or concomitant elevation in the atrial and pulmonic pressures than that seen in the rest. As a matter of fact, the elevation was less significant than in those which were not so supported.

The foregoing experimental work (presented in complete detail elsewhere[17, 18]) indicates that the suggested procedure was consistently effective in eliminating artificially produced mitral regurgitation; that this operation can be performed with reasonable safety eliminating some of the early pitfalls and hazards; that no significant damage was done to the heart when the technique was properly carried out. The major danger of this procedure is that of erosion of the suture into the lumen of the atrium. This complication was eliminated entirely by the simple modifications of the original technique described. It is further shown that the degree of circumferential constriction herein employed, even of the normal dog's atrioventricular ring, produced only insignificant hemodynamic alterations.

Past experience, both in the surgery of mitral stenosis and in the study of pathologic specimens, led us to believe that this principle was likely to be effective in a significantly large proportion of cases with mitral insufficiency. On this basis, limited clinical trial of the operation was considered justified.

INITIAL CLINICAL TRIALS

To the present time, 7 patients in very severe states of marked to intractable chronic congestive failure associated with obvious mitral regurgitation have undergone surgery by this technique. The salient features of these cases will be given here, pending a detailed report after a more adequate follow-up period has elapsed.

CASE 1.—R. M., a 28-year-old white woman, was operated upon on Jan. 20, 1955, with a diagnosis of predominant mitral stenosis, mitral insufficiency, and adynamic aortic stenosis. Atrial fibrillation was present. She had a history of rapidly progressing congestive failure unresponsive to medical care.

At surgery, the diagnosis of aortic stenosis was ruled out by direct examination and by pressure determinations in the aorta and left ventricle. The left ventricular systolic pressure was 100 mm. Hg and the aortic pressure, just distal to the valve, was 110 mm. Hg. The pressure in the left atrium was 30/10 (17) mm. Hg. Digital exploration of the mitral valve revealed a marked mitral insufficiency with a Grade 3 regurgitant jet. The orifice could admit 2½ to 3 fingers. The leaflets were thickened but very pliable. They were held taut by the shortened chorade tendineae and the greatly enlarged ring. The commissures were rounded and slightly scarred and fused. Although this was not the original plan, placement of a circumferential suture was undertaken in view of the ideal type of valve deformity and the rapid downhill clinical course.

The technique followed was identical with that which has been described experimentally. Although there was tremendous enlargement of the left atrium and moderate to marked enlargement of the left ventricle, the procedure was carried out with surprising ease. As the suture was tied, the intra-atrial finger palpated a gradual and dramatic disappearance of the regurgitant jet. The ring was drawn down to a diameter of approximately 5 cm. (2½ to 3 fingers). The tense leaflets relaxed and were able to move freely, retracting adequately to allow an effective orifice of at least 2 fingers. The continuous electrocardiographic monitor was observed during the procedure and the only unusual change noted was a slight, transient decrease in voltage of the QRS complex. The tension within the left atrium and the marked

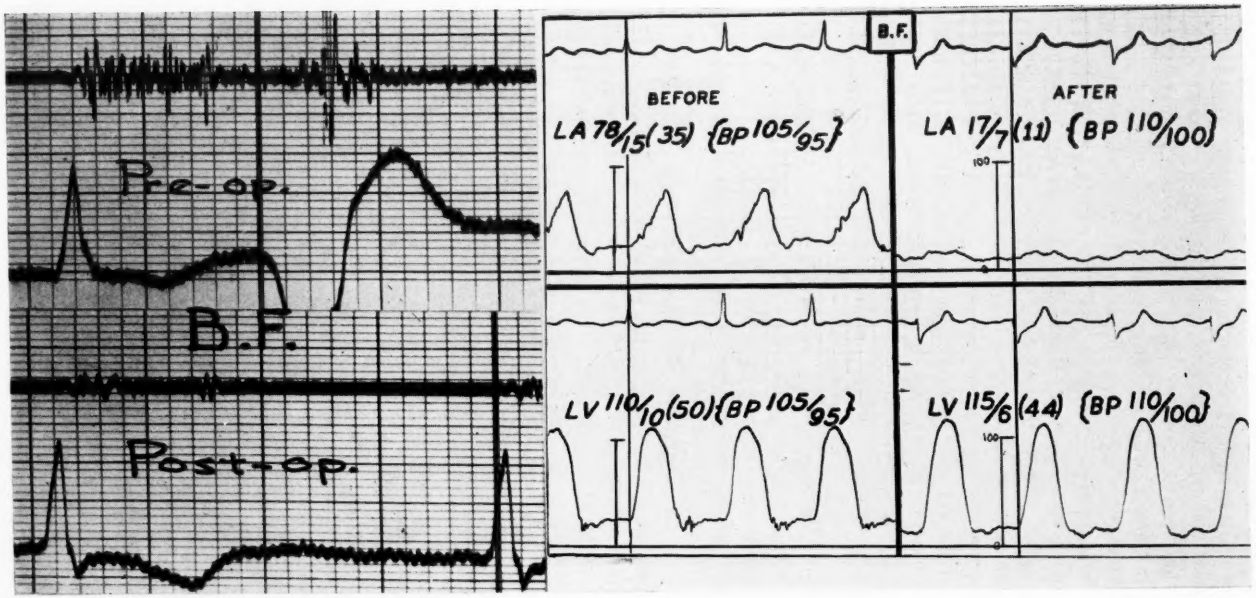

Fig. 13.—Case 2. Left: pre- and postoperative phonocardiogram. Right: pre- and postoperative left atrial, and left ventricular pressure pulses. Note the change in contour as well as in pressure. The S-T segment depression seen in the electrocardiogram tracings during this recording was transient.

dilatation of the ventricle decreased visibly within a few beats after the suture had been tied. There was an obvious redundancy and flaccidity of the greatly enlarged atrial chamber. Further digital exploration revealed a barely palpable "whiff" of regurgitation in the posterior commissural region. Pressure tracings were repeated showing a drop in the left atrium to 19/7 (11) mm. Hg. The left ventricular pressure was now 112 mm. Hg systolic. Blood loss and tolerance to the procedure were comparable to that of the usual mitral commissurotomy.

Postoperatively, the patient had an uneventful recovery. Daily electrocardiograms showed no significant change. The x-rays of the chest revealed a significant decrease in the size of the heart within one week of surgery. The mitral systolic murmur had changed from a preoperative Grade 3 to a Grade 1. She was discharged on Feb. 9, 1955 (twentieth postoperative day). Her last visit was on April 18, 1955, at which time she stated that she had been doing all her housework, except laundry, for the past three weeks. She had felt very well, had no shortness of breath, and had been sleeping flat in bed. She continues to take digitoxin. X-rays showed persistence of the decrease in the cardiac size. The electrocardiogram remained unchanged except for marked digitalis effect. The phonocardiogram revealed a persistent, mitral systolic murmur but greatly reduced in amplitude and duration. No mitral diastolic murmur was demonstrable.

CASE 2.—B. F., a 24-year-old white woman, who had a previous mitral valve exploration in 1953, was operated upon on Feb. 1, 1955. The preoperative diagnosis was predominant mitral insufficiency with auricular fibrillation and intractable congestive heart failure.

At surgery, the heart was found to be of tremendous size, the largest which any of us had seen. The atrium was easily the size of a soccer ball. The pressures in the left atrium were 78/15 (35) mm. Hg, in the left ventricle 110/10 (50) mm. Hg, in the pulmonary artery 110/65 (84) mm. Hg. Exploration of the mitral valve through a rubber "appendage" sewn onto the anterior atrial wall revealed a ring which was enlarged to 4 or 5 fingers. The valve leaflets were shortened, tensed, and slightly thickened but quite pliable. There was no stenosis. The Grade 4 regurgitant jet was felt in all areas of the mitral orifice. The effective orifice was easily 3 to 4 fingers. The circumferential suture was placed using the same technique. Here, however, the situation was complicated by the previous cardiac exploration which had resulted in pericardial scarring to the extent that it was difficult to identify with confidence the lateral coronary artery branches. Nevertheless, it was possible to place the purse-string suture without evident injury to these vessels. Difficulty was also experienced in the maneuver of threading the Reverdin needle as it emerged into the transverse sinus. The size of the heart made it necessary to exert considerable upward traction on the needle to make the threading of it possible. The regurgitant jet diminished becoming barely detectable and localized to the region of the posterior commissure. The size of the left ventricle decreased markedly and promptly. The tension in the atrium also diminished until it became a flaccid sac. Tracings now revealed an atrial pressure of 17/7 (11) mm. Hg, 125/5 (47) mm. Hg in the left ventricle, 102/59 (75) mm. Hg in the pulmonary artery. A transient depression of the S T segment in Lead II was the only electrocardiographic change noted during the operation.

Immediately postoperatively the patient was hypotensive requiring vasopressor drugs. It was necessary to administer positive pressure oxygen for two to three hours. In twenty-four hours the vital signs were stabilized. Thereafter the major difficulty consisted of excessive tracheobronchial secretions requiring mucolytic vaporization. After the third postoperative day, her course was uneventful except for three or four episodes of epistaxis which necessitated cauterization of the bleeding area. The preoperative ascites disappeared in the succeeding three weeks. The liver receded from the level of the iliac crest to 2 finger-breadths below the costal margin. Daily electrocardiograms showed no abnormalities which had not been present preoperatively (atrial fibrillation and premature ventricular contractions). The phonocardiogram showed barely detectable systolic vibrations (Fig. 13), although a Grade 1 systolic murmur was audible. She was discharged on the nineteenth postoperative day, Feb. 20, 1955, and returned to her home in Ohio. On April 4, 1955, we received a report from her attending physician that she had returned home in very good condition. However, within

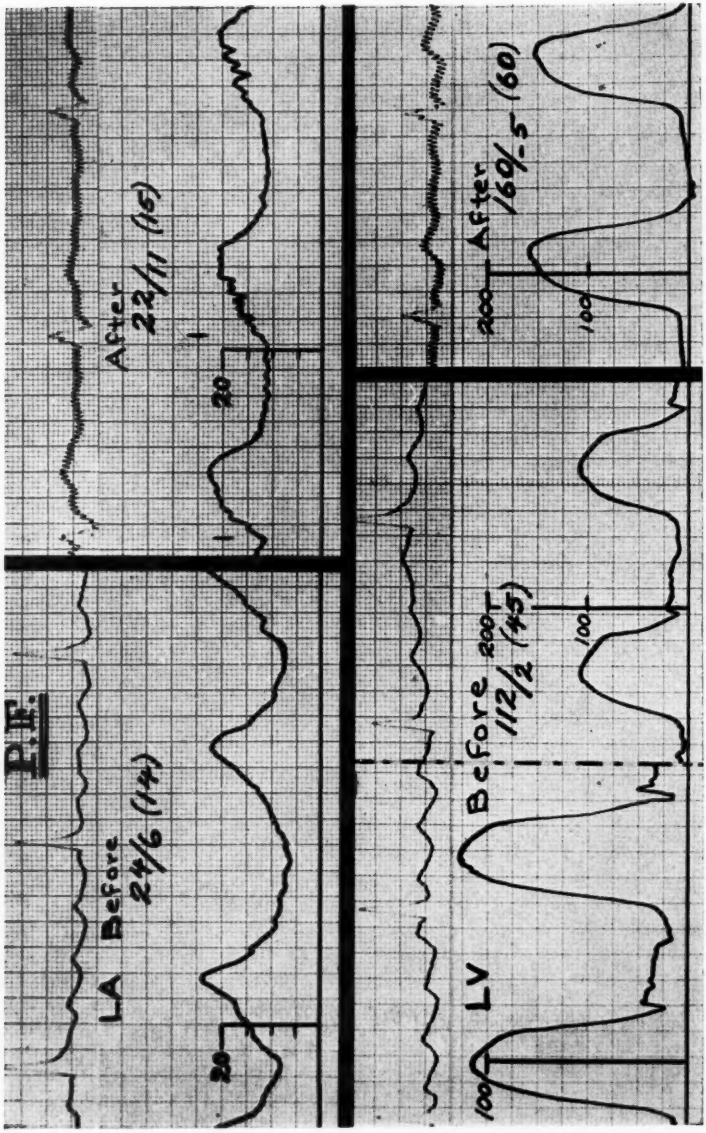

Fig. 14.—Case 3. The pre- and postoperative pressure pulse tracings of the left atrium and ventricle are shown. The negligible change in the atrial pressure is due to the fact that this patient had a severely calcified valve with stenosis and regurgitation which was seriously aggravated by commissurotomy. The postoperative pressures and contours indicate that the regurgitation was diminished significantly. The inability of the leaflets to regain a satisfactory degree of motility despite an adequate commissurotomy, actually indicates possible persistence of a stenotic effect despite the fact that the effective orifice could admit 2 fingers.

one week, ankle edema and progressive right heart failure returned, necessitating frequent mercurial diuretics. Her cough returned and she had minimal hemoptysis and slight fever. Antibiotics improved these symptoms in a "few days." The heart sounds had not changed. During the last week, she gradually became anuric and an increasing degree of ankle edema and hepatomegaly were noted. She died on April 1, 1955. An autopsy was not performed.

CASE 3.—P. F., a 27-year-old white woman, was operated upon on Feb. 24, 1955. The diagnosis was predominant mitral insufficiency with adynamic mitral stenosis, aortic stenosis, atrial fibrillation, and severe congestive failure.

At surgery the heart was found to be very large. There was a Grade 1 systolic thrill at the aortic valve. There was little deformity of the aortic valve as palpated externally. The pressure gradient across it was 30 mm. Hg. The left atrial pressure was 24/6 (14) mm. Hg and that of the left ventricle was 112/2 (45) mm. Hg. The mitral valve was stenosed and insufficient. The effective orifice admitted 1 to 1½ fingers. There was considerable calcification in the region of the posterior commissure. The leaflets were moderately pliable although thickened and rolled. The annulus was only moderately enlarged. There was a Grade 3 regurgitant jet. A commissurotomy was planned after placement of the mitral purse-string suture. As the Reverdin needle was being manipulated around the annulus, the heart went into ventricular fibrillation. The needle was withdrawn at once. After twenty-two minute of cardiac massage, multiple shocks, and administration of drugs, the heartbeat was restored. At a second attempt, the circumferential suture was easily placed and subsequently the anterolateral commissure was opened. The regurgitation was considerably increased by the commissurotomy. The purse-string suture was then tied, constricting the annulus to a size compatible with that of 2½ to 3 fingers. The effective orifice of the valve now would admit at least 2 fingers. The very severe degree of regurgitation decreased to the point where only a small jet could be felt in the region of the posterior commissure. Although the major part of the leaflets moved better after the operation, motion in the region of the posterior commissure was not greatly improved. The left atrial pressure was now 22/11 (15) mm. Hg and in the left ventricle 160/–5 (60) mm. Hg. Although this represents a negligible change in the left atrial pressure, the change in ventricular pressure and the difference in the atrial and ventricular pressure pulse contours are indicative of considerable reduction of the regurgitation (Fig. 14). Postoperatively, the patient did quite well despite a short interval during which hypotension required supportive measures. A left pleural effusion necessitated thoracentesis. The systolic murmur decreased considerably in intensity and the diastolic murmur likewise decreased in intensity. The postoperative x-rays showed slight decrease in size of the cardiac silhouette. The electrocardiogram did not reveal any abnormalities which were not noted preoperatively. The patient was discharged on March 30, 1955 (thirty-fourth postoperative day), and was last seen on April 14, 1955, at which time she stated that she felt better than she had "in years." She has been inactive as instructed and continues to take digitoxin. She has been completely free of the dyspnea, orthopnea, and ankle edema which she had preoperatively under this same regime.

CASE 4.—B. W., a 41-year-old woman, was operated upon on March 1, 1955, with the diagnosis of predominant mitral regurgitation with stenosis, adynamic aortic stenosis and insufficiency, chronic intractable congestive failure.

At surgery, an enormous heart was found with a huge, tensed left atrium and a large, pale left ventricle. There was induration about the aortic valve and a moderate degree of poststenotic dilatation. Pressure in the aorta was 130/55 (90) mm. Hg, in the left ventricle 155/–2 (55) mm. Hg, in the left atrium 28/11 (17) mm. Hg, and in the pulmonary artery 54/25 (37) mm. Hg. The mitral valve was badly calcified with an effective orifice which barely admitted 1½ fingers. The cusps were fixed, tensed, and rigid. The ring was only moderately enlarged. There was a Grade 2 regurgitant jet. The anterolateral commissure was opened widely out to the myocardium. Since this improved the stenosis only partly because of the fixation of the leaflets, the posterior commissure had to be opened also. This required cutting through solid calcium. The leaflets could now open to an effective orifice which could have admitted 2½ fingers. However, there was now a Grade 4 regurgitant jet. A circumferential suture was placed and tied until the jet

decreased in intensity to a Grade 1 or less. The effective orifice would still accommodate 2½ fingers. Aortic valve dilatation was considered but discarded in view of the stage of disease of the myocardium and in the face of a gradient which could probably not have been improved much. Pressures after the procedures were taken. In the left atrium it was now 17/6 (11) mm. Hg, in the left ventricle 150/–2 (55) mm. Hg, in the aorta it was 100/62 (80) mm. Hg, and in the pulmonary artery 54/26 (37) mm. Hg (Fig. 15). The immediate postoperative course was stormy. The urinary output was markedly depressed during the first three days. She was hypotensive and slightly cyanotic for about twenty-four hours.

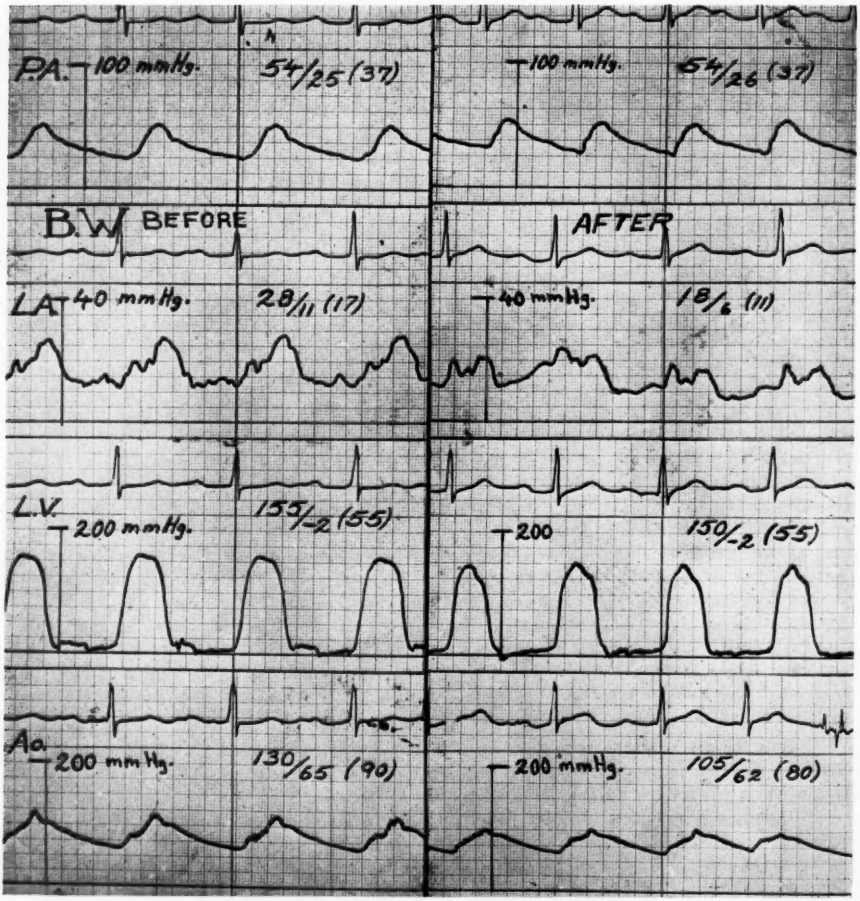

Fig. 15.—Case 4. Pressure pulse tracings pre- and postoperatively of pulmonary artery, left atrium, left ventricle, and aorta. Note the stenotic contour of the aortic curve.

This situation gradually improved and by the end of the first week the urinary output was adequate and the blood pressure stable. The daily electrocardiogram revealed no significant changes compared to the preoperative tracings. During the third week, she gradually became cyanotic, dyspneic, and edematous. A moderate electrolyte imbalance was noted. The liver became enlarged after having receded rapidly after surgery. The patient died on March 22. 1955 (three weeks postoperatively).

At autopsy, the heart was found to be enormous. The surgical wounds of the heart were healing quite well. There was extensive mitral valve disease as noted at operation. The degree of aortic stenosis was compatible with the evaluation made at surgery. In addition, there was a tremendous degree of organic tricuspid insufficiency. The lungs were congested and fibrotic and showed several small areas of consolidation which could have been small infarcts. The liver was extremely large and showed marked cirrhotic changes. The commissurotomy was adequate. The valve cusps were rigid and required pressure to depress them. The circumferential suture was well placed, had elicited minimal gross tissue reaction, and had not eroded through the encircled tissues. There was no evidence of myocardial infarction. The segment of suture lying in the right atrium adjacent to the septal surface was completely covered over by a translucent layer of glistening endotheliumlike tissue. There were no foci of thrombosis in the heart, except for a small adherent thrombus in the dimple of the left atrial appendage stump.

CASE 5.—L. T., was a 19-year-old woman who was operated upon on March 3, 1955, with the diagnosis of mitral insufficiency, auricular fibrillation, massive cardiomegaly, and intractable congestive failure.

At surgery, the left atrium was found to be the largest of all seven cases. The left ventricle was enormous and pale. The pressure in the left atrium was 38/5 (19) mm. Hg, in the left ventricle 102/–5 (38) mm. Hg, in the aorta 100/80 (87) mm. Hg, and in the pulmonary artery 110/70 (82) mm. Hg. There was no detectable aortic valve disease. The mitral valve was found to be pliable although somewhat thickened. There was Grade 4 regurgitant jet. The annulus could have easily admitted 5 fingers and the effective orifice at least 3 fingers. As preparations were made for placement of the mitral purse-string suture, ventricular fibrillation ensued. Placement of the suture had not been started. Massage was noted to be very inefficient because of the massive mitral regurgitation. However, after repeated shocks, drugs, and massage, a weak beat was restored. It was decided that correction of the regurgitation was imperative and therefore placement of the suture was undertaken. At the moment that this was begun ventricular fibrillation returned. The circumferential suture was then placed while cardiac massage was carried out. Constriction of the ring could be felt to practically eliminate the regurgitation. At this point the thinned-out left atrial wall tore, resulting in considerable and rapid blood loss. After attempts to control bleeding and continued massage and resuscitation measures failed, the patient was pronounced dead.

An autopsy revealed an ideal valve for this method of correcting regurgitation. There was extensive pulmonary and hepatic damage and the myocardium was obviously of very poor quality. This specimen was studied on the pulse duplicator[19] with which cinematographic studies were made demonstrating clearly the correction of the regurgitation by the circumferential suture.

CASE 6.—R. S., a 28-year-old woman, was operated upon on April 19, 1955, with the diagnosis of mitral insufficiency, atrial fibrillation, and chronic intractable congestive failure.

At surgery a very large heart was found. The pressures taken in the left atrium were 20/–3 mm. Hg, in the left ventricle 90/–8 mm. Hg, and in the pulmonary artery 22/12 mm. Hg. Exploration of the mitral valve revealed a greatly dilated ring which could have admitted 4 to 5 fingers. The leaflets were thickened but moderately pliable. There was a plaque of calcium in the mid-portion of the anterolateral leaflet. The effective orifice could admit 3½ fingers. The circumferential suture was placed easily using a new needle especially designed for this procedure. This instrument facilitates threading and eliminates the need for cardiac dislocation during this maneuver. Tying of the suture reduced the ring to a size which could admit 3½ fingers and the effective orifice would still admit 3 fingers. The leaflets which were tense and immobile now moved freely. The Grade 4 regurgitant jet became a negligible faint posterior "whiff." The left atrial pressure was now 5/–4 mm. Hg, in the left ventricle 92/–10 mm. Hg, and in the pulmonary artery 24/7 mm. Hg.

The patient has had an uneventful and smooth postoperative course. The electrocardiogram shows no significant change in the first three postoperative days. There is now a faint mitral systolic murmur as compared to the Grade 4 preoperative murmur.

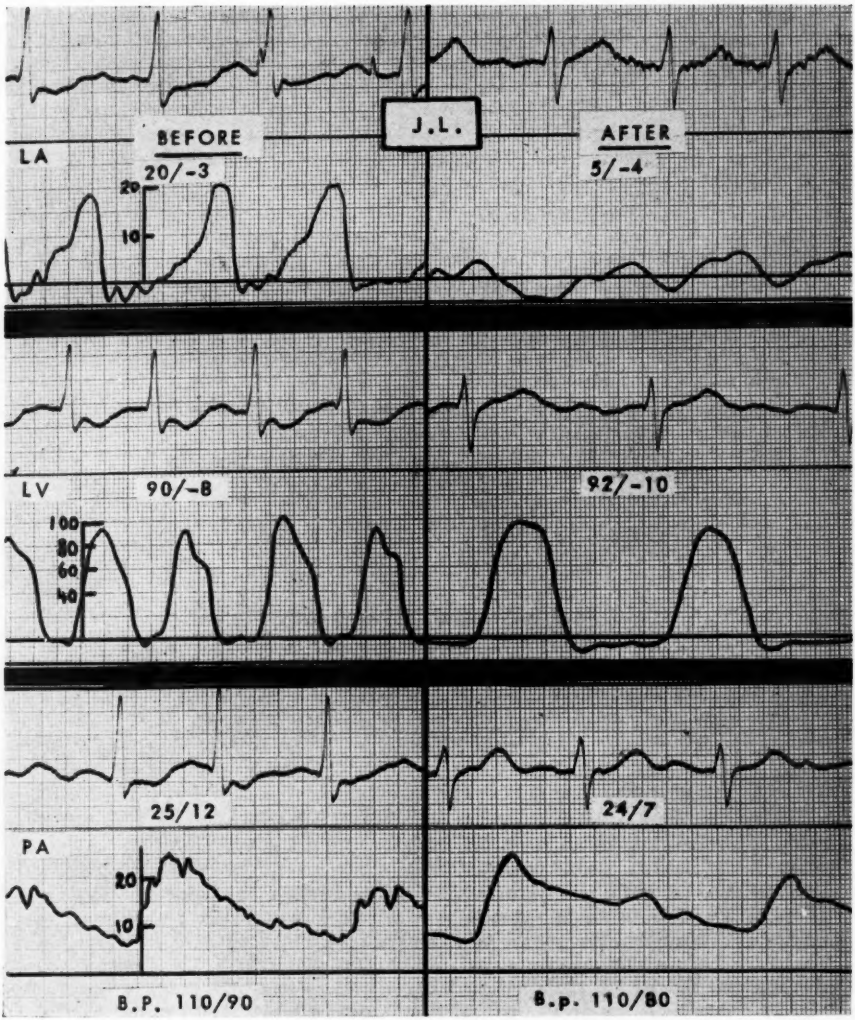

Fig. 16.—Case 7. Note the remarkable changes in pressure and contour of both the atrial and ventricular pressure pulse tracings. The change in the electrocardiogram was transient.

CASE 7.—J. L., a 25-year-old woman, was operated upon on April 21, 1955, with the diagnosis of mitral insufficiency, atrial fibrillation, moderate left ventricular hypertrophy, and she had a previous history of subacute bacterial endocarditis. At surgery a very large heart was found. The pressure in the left atrium was 27/0 mm. Hg, and 80/–8 mm. Hg in the left ventricle. The mitral valve leaflets were thickened but quite pliable. The annulus was large enough to have admitted 5 fingers, the effective orifice 3 to 3½ fingers. The circumferential suture was placed easily with the new instrument and tied, reducing the annulus to a size compatible with 3 to 4 fingers. The tense, shortened leaflets were felt to relax and to come together easily in systole. The Grade 4 regurgitant jet changed to a barely perceptible "whiff." The effective orifice still could have admitted 3 to 3½ fingers. Pressures were repeated and found to be 10/0.5 mm. Hg in the left atrium, and 96/–4 mm. Hg in the left ventricle.

Postoperatively the patient had retained secretions requiring tracheal aspirations. A hypotensive state was controlled with norepinephrine. Her condition at the time of this report is fair and showing gradual improvement.

SUMMARY AND CONCLUSIONS

The rationale of circumferential suture of the mitral valve for the correction of mitral insufficiency is reviewed and discussed.

The results of experimental studies in the production and correction of mitral insufficiency as well as in the study of the problems associated with the development of the technique are reviewed and summarized.

Preliminary reports of the first 7 patients in whom this procedure has been tried are given.

The experimental work demonstrates that the regurgitation produced artificially can be eliminated. The procedure for circumferential suture or purse-string suturing of the mitral annulus has been perfected and in its present form has proved to be relatively simple and safe. When properly performed, no significant damage to the cardiac conduction system, the coronary circulation, or the muscle itself can be demonstrated. No significant hemodynamic alterations can be attributed to the procedure in the experimental animals. Mitral stenosis is not produced.

Limited clinical trial in 7 severely ill patients demonstrated objectively and clinically that regurgitation associated with rheumatic heart disease can be corrected.

The final results of this procedure would appear, at this time, to depend upon the pathologic state of the valve. The myocardial, pulmonary, hepatic, and renal status of the severely ill patients who have been operated upon appears to be the major cause of death in the 3 patients we have lost. For the immediate future, continued clinical trial seems clearly justified. Until further experience has been acquired, however, the procedure should be applied only in critically ill patients.

It must be pointed out that although the technique in its present form is simple and easy to perform, a preliminary study of the pertinent anatomy and practice on experimental animals will be essential for its proper performance.

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DISCUSSION

DR. RALPH A. DETERLING, JR., New York, N. Y.: I arise to mention a patient in whom my colleague, Dr. F. F. McAllister, in August, 1954, employed an annular purse-string suture of cotton braided tape for control of mitral insufficiency. She has had definite clinical improvement, although the x-ray of the heart has not shown significant change.

DR. CHARLES P. BAILEY, Philadelphia, Pa.: As you can well imagine, having been responsible for the so-called "sash operation" for aortic insufficiency due to annular dilatation, we are very much interested in the operation proposed by Dr. Davila and his associates.

(slide) This sash goes under both coronary arteries, through both atrial chambers, and between the pulmonary conus and the aorta.

(slide) The one significant difference in application is that in our procedure the sash is put directly about the aortic annular level. On the other hand, the mitral annulus laterally is found pretty close to the atrioventricular junction, and in cases of annular dilatation becomes displaced upward away from the apex. So the external portion of the constricting suture that Dr. Davila is using, since it lies within ventricular wall tissue, is placed significantly below the anatomic level of the annulus.

(slide) The medial portion of the suture is placed outside the trigone, but actually this is not the region in which the inner portion of the annulus should be. Of course, it can be put there and I do not mean to criticize their technique, but wish to point out something that we have observed in our own experience with the aortic valve, that I think would undoubtedly be pertinent here.

(slide) Here is the brachial artery tracing in a patient with severe aortic insufficiency, during surgery immediately before applying the sash. Here is the change in the brachial arterial pressure tracing brought about by tightening the sash. We obtained a nice diastolic elevation and practically a normal contour.

(slide) Two weeks later when we reoperated on him, you see the reversion of the pressures in the brachial artery, a change to a condition of considerable restoration of insufficiency. Further tightening of the sash, as you see, changed the condition to one indicating some stenosis but relief of the regurgitation.

The reason for the observed early loss of constriction is that soft tissue lying between the sash and the annulus cuts through gradually from the pressure against the underlying aorta or ventricle. Since much larger amounts of muscle mass are included within the constricting suture in Dr. Davila's method of tightening the mitral annulus, it would seem to me that loss of restraint due to such pressure necrosis must necessarily be much more pronounced. Perhaps improvement in the technical details will overcome that difficulty, which I think otherwise must cause loss of the effect of overcoming regurgitation.

DR. MARK M. RAVITCH, New York, N. Y.: We are very glad to hear that Dr. Glover and his associates have found a practical and satisfactory method of approximating the lips of the annulus. This problem is being studied in our laboratory by Dr. Robert Wilder and Dr. Howard Moscowitz, whose work it is that I am showing.

(slide) One of the risks involved in such a circular suture, of course, is that one is producing a controlled type of mitral stenosis. Here is a tracing of atrial, ventricular, and aortic pressures in a normal dog; here a tracing in a dog with mitral insufficiency, with a sloping systolic rise in auricular pressure; and here a mitral stenosis of considerable degree with a sharp gradient across the valve and higher auricular than ventricular pressure in diastole.

(slide) When one starts to operate in an animal with mitral insufficiency, and cinches down with a purse-string suture above the annulus, one produces, as one might expect, a characteristic stenosis of variable degree, and the problem may be one of producing a controlled stenosis which will not ultimately become dynamically significant. The motion picture strip which we have will demonstrate another method of investigating the mechanics of mitral insufficiency. For orientation purposes, the next slide shows you the appearance of a percutaneous injection of radiopaque material into the left ventricle, demonstrated by an ordinary spot film.

(slide) This shows a dog with mitral insufficiency; you see the auricle filled with dye, the left ventricle, the sinus of Valsalva.

(slide) This shows a competent mitral valve, and I would urge you to watch the motion picture for a thin black line which appears to be the annulus; it may represent the accumulation of a little contrast medium under the edge of the annulus.

(Motion Picture) This is an ordinary catheter angiocardiogram, for orientation. Here is the right side of the heart and you see the pulmonary artery coming down, the left auricle and left ventricle filling, and the aorta. Notice, by the way, how long it takes for the heart to empty, and how irregular the admixture appears. Here is the needle being placed into the left ventricle. There is the mitral ring and the little line; notice the blood swirling around the ventricle and swept away by the leaflets of the valve. Here is an intact mitral valve. Note the straight ventricular border at the line of valve closure. This is an insufficency of relatively major degree, and the next is another major insufficiency, much the same kind. It is so great that you cannot actually see the reflux of the contrast medium, you can simply see the auricle fill rapidly. The next animal had a very minor degree of insufficiency, and you can see here a little swirl of dye shooting up in a little jet, around the back of the auricle.

Dr. Wilder and Dr. Moscowitz also studied the problem with respect to auricular fibrillation produced by aconitine and it would appear from repeated study of such films that in such auricular fibrillation there is a minor degree of mitral insufficiency.

This is a very simple examination and may serve to indicate a possible method of diagnosing mitral insufficiency and assessing the value of a corrective procedure. The motion pictures are taken with the Phillips screen intensifier.

DR. HARRISON BLACK, Boston, Mass.: I would like to congratulate Drs. Davila, Glover, and associates on the very excellent presentation of correction of mitral insufficiency as shown in the movies of the perfused heart. On Dr. Harken's services, in Boston, we have also been impressed with the potentialities of constricting the annulus of the mitral valve for correction of regurgitation. In fact, a different method of achieving annulus distortion was included in our report on the correction of mitral insufficiency before this Association last year. Implicit in this approach is an appreciation of the fundamental importance of avoiding interference with leaflet mobility that we have stressed many times in the past.

I would like to add a three-dimensional concept of the dynamic pathology of pure mitral insufficiency that has evolved from our studies of this condition. In addition to loss of leaflet substance due to the rheumatic process and the ensuing dilatation of the annulus, there occurs a sliding hernia of leaflets over the fibrous annulus further shortening them and rendering them more incompetent. This alteration develops because of the aneurysmal dilatation of the left atrium which sags downward toward the diaphragm. This observation has been independently made by Edwards of the Mayo Clinic. We have found that external bolstering of the aneurysm of the left auricle can correct, to a certain degree, this sliding hernia of the leaflets and reduce or correct mitral regurgitation at the operating table. Some attention to this factor will probably play a role in our eventual methods for correction of mitral regurgitation.

Another approach, which is currently under investigation in our laboratory, is to plicate the mitral annulus posteriorly under direct vision in the opened left auricle during hypothermia. Whichever of these methods eventually proves the most useful, the principle of bringing the leaflets into approximation by reducing the size of the annulus appears to be promising.

DR. EARLE B. KAY, Cleveland, Ohio: I should like to congratulate Dr. Davila and Dr. Glover on their very excellent presentation. We have also employed the concept of the dilated mitral annulus in the surgical correction of mitral regurgitation. It is our interpretation that after the annulus once dilates as a result of left ventricular hypertrophy and dilatation, this becomes the most significant factor in the perpetuation of this entity.

(slide) In pure mitral insufficiency, the regurgitant stream of blood can be detected by the intracardiac finger being directed through the separated posterior medial commissure toward the atrial septum and posteriorly. This regurgitant flow can be entirely eliminated if pressure is exerted upward by a finger placed posteriorly at the atrioventricular ring. Such pressure decreased the size of the dilated ring and separated posteromedial commissure. We have found that this same sequence of events can be accomplished by inserting a suture, followed later by a tubed pericardial graft based anteriorly through first the anterior segment of the dilated annulus adjacent to the posteromedial commissure, then through the posterior segment of the annulus, and to exit posteriorly on the ventricular side of the coronary sinus. This graft is brought through an opening in the posterior pericardium, to which it is sutured after the optimum degree of tautness is obtained by the assistant pulling on the graft with one hand and pushing upward on the posterior aspect of the heart with the other, as directed by the surgeon's intracardiac finger.

We have operated upon 7 patients with the past year employing this technique. There were no operative deaths. Two patients died later; 1 several days after leaving the hospital, from what was thought to be a pulmonary embolus, and the other four months later from progressive multivalvular disease.

DR. DAVILA (Closing).—Several points were brought up which I thought might be answered now, or at least clarified. The first concerns the level of the purse-string suture when it is placed. It is not below the ring; it lies actually, if anything, a little above the ring, because the suture seems to find its way into the groove adjacent to the ring as it is tied.

It remains there and specimens, as long as six months after the operation was performed in dogs, have shown that the size of the constriction remains the same as when originally performed.

Dr. Kay has presented a very interesting procedure which brings up a question concerning the danger of material placed across the lumen of a chamber. In some of our dogs originally, when we were having trouble with the suture cutting through, a cord of silk would lie across the lumen of the left atrium, and we had a tremendous incidence of embolic accidents in these animals.

One other point in connection with partial constriction procedures of the ring is that they are only partial. The total encirclement of the ring has the additional advantage that potential further dilatation of the ring, in a case in which total regurgitation has not been eliminated, will be prevented from producing the progressive enlargement of the ring, of which we are all aware. Mitral stenosis was of course a very prominent concern in this study. We have found a slight to moderate elevation in the left atrioventricular gradient in the acute state in the dogs in which we have done this procedure. It must be remembered that experimentally one is constricting a ring of normal size. The elevation which has been seen in the dogs has not been seen in the patients in whom this procedure has been performed. We do not think that mitral stenosis, when the procedure is performed adequately, will be a significant hazard.

The delay in emptying of the left heart in the angiocardiograms shown by Dr. Ravitch is an interesting point. In our pulse duplicator we injected dye into the chambers of a heart with mitral regurgitation as it was pumping. One could obviously see a very prolonged delay in emptying of the left heart. This has promise as a possible valuable diagnostic measure.

STUDIES ON THE FUNCTION OF THE HUMAN VAGUS NERVE IN VARIOUS TYPES OF INTRATHORACIC DISEASE

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EMORY UNIVERSITY, GA.

A CONSIDERABLE interest in the problem of the function of the autonomic nervous system in relation to the various types of pulmonary pathology has been expressed in previous publications by our group.[1-5] Our studies have impressed upon us the need for detailed investigative studies relative to the function of the human vagus nerve in various disease states which involve the intrathoracic organs.

A sizable literature has accumulated relative to physiologic studies upon the right ventricular and pulmonary arterial pressure in chronic pulmonary emphysema and pulmonary fibrosis. To our knowledge, these studies have been confined to cardiac catheterization techniques in patients with an intact chest wall. Recently, a cumulative group of studies has been presented relative to both cardiac catheterization studies, direct intracardiac, and direct intracardiac and pulmonary vascular pressure measurements in various types of cardiac defects. An excellent review of such findings can be read in the recent monograph of Altschule.[6]

A brief review of the knowledge concerning right ventricular and pulmonary vascular pressures in pulmonary fibrosis and chronic pulmonary emphysema seems merited. In pulmonary fibrosis, the right ventricular and pulmonary arterial pressures are normal or elevated.[7-10] An excessive rise in pulmonary artery pressure during exercise is characteristic.[11, 12] Anoxia occurred as a definite factor in the elevation of pulmonary arterial pressure in pulmonary fibrosis.[9, 13, 14] A normal pulmonary capillary pressure is usually seen.[9, 13]

The findings in pulmonary emphysema reveal that the right ventricular pressure may be normal or high,[6, 7, 15] and an excessive rise during effort may be noted.[17] In a similar fashion, the pulmonary artery pressure may be elevated.[15, 18-20] Fowler,[21] in 1950, suggested a neurogenic mechanism for this phenomenon when he revealed that tetraethylammonium chloride lowers an elevated pressure without changing the pulmonary capillary pressure (which was normal to begin with). Pulmonary artery pressure rises with exercise whether initially normal or elevated.[11, 18] Yu and his associates[22] have suggested that pulmonary hypertension may be related to both anoxia and hypercarbia. Normal right auricular pressures and pulmonary capillary pressures have been reported.[22] A postural effect has been noted in that the pulmonary

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arterial pressure is lower in the erect than in the supine position in patients with emphysema but not in normal subjects.[23]

PURPOSE AND PLAN OF THE EXPERIMENT

The fundamental purpose of the experiment is an attempt to increase our basic knowledge concerning the physiologic and the pathophysiologic function of the human vagus nerve in relation to pulmonary vascular dynamics.

There have been two fundamental experimental plans involved. First, a group of patients having certain pathologic pulmonary states have been studied by cardiac catheterization while conscious and with the chest wall intact. The

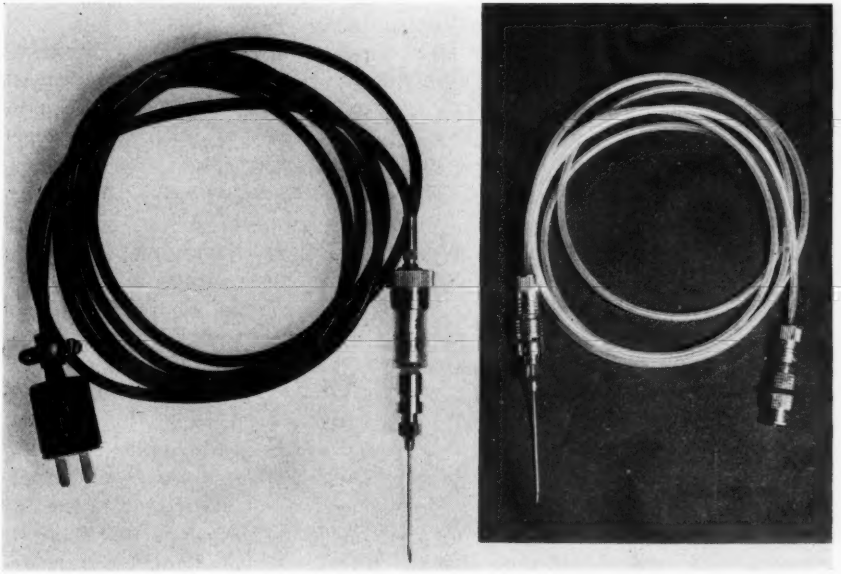

Fig. 1.—Type of equipment used for direct measurement of intraluminal pressures at thoracotomy. At the left is a Hathaway reluctance pressure transducer. At the right is a simple plastic catheter (filled with saline) attached to a Sanborn strain gauge manometer. All pressures were recorded on a Sanborn "DuoViso Cardette."

effect of parasympathetic paralyzing drugs upon the right ventricular and pulmonary arterial pressures in such patients has been studied. In a second group of patients (Fig. 1), studies have been carried out upon the effect of (a) direct unilateral vagus nerve block with 1 per cent Novocain, and (b) pharmaceutical block (atropine sulfate) upon direct pulmonary arterial and pulmonary venous measurements at the time of thoracotomy in various pathologic pulmonary and cardiovascular conditions.

DETAILS OF EXPERIMENTAL METHOD

In the first group, a standard cardiac catheterization technique was incorporated, not involving the preliminary administration of any drugs. Particular attention was paid to obtaining baseline measurements of the right ventricular and pulmonary arterial pressures, both at rest and with a standard exercise

test. The time for return of an elevated pressure, after exercise, to the original base line was recorded in several instances. Similar measurements were then repeated within the same cardiac catheterization after the intravenous administration of certain drugs known to have the capacity of producing a pharmacologic block of the vagus nerve. In one group of patients, 30 mg. of Pro-Banthine was given, and in another, 0.65 mg. of atropine sulfate was administered. Following the catheterization, a comparison of the pressure measurements at rest and during exercise was made in all patients. In a small group of patients, the time required for an elevated pressure, with exercise, to return to normal before and after the vagal blocking agent was analyzed.

In certain instances, patients who had undergone preoperative cardiac catheterizations of this type were subsequently studied by direct pressure measurements of the pulmonary artery and/or pulmonary vein at the time of thoracotomy. A comparison of such studies will be included in a later communication. Furthermore, in some instances, concomitant pressure studies of the pulmonary vein and pulmonary artery were accomplished, but the number of such studies is still too limited to warrant description at this time.

In the second group of patients, direct pressure measurements were carried out by the introduction of a No. 18 or a No. 20 gauge needle directly into the pulmonary artery just before its lobar or segmental branching. In other patients, direct pressure measurements were carried out in either the superior or inferior pulmonary vein before its entry into the pericardial sac. In all but one patient, the operative position was either the right or left lateral decubitus. In one instance, measurements in the face-down (Overholt) position were carried out.

A sincere attempt to standardize the baseline conditions of the patients was incorporated throughout the study. Similar preoperative sedation, involving morphine sulfate and barbiturate, was maintained and no studies were performed less than two hours after such preoperative medication. The time of administration of a standard dose of atropine sulfate (which in this Clinic is given intravenously at the time of induction with Pentothal sodium) was recorded. Pressure measurements were taken at least seventy-five minutes following the administration of the induction dosage of atropine. The type of anesthesia was constant throughout and incorporated Pentothal sodium or Surital induction, production of apnea by succinyl choline chloride (Anectine), and maintenance of apnea by slow drip of this drug. Nitrous oxide (65 per cent) and oxygen (35 per cent) were given to maintain analgesia and adequate oxygenation. In all instances, endotracheal intubation with positive pressure was used. A constant and controllable ventilatory pressure was maintained with the Rand-Wolf Respiratory. The direct intravascular pressure measurements were made satisfactorily after the vessel was first isolated for study. In patients in whom a direct vagus nerve block was incorporated, the vagus nerve was dissected out so that it could be injected under direct vision at a level at least 3 cm. above the bifurcation of the trachea. Intravascular pressure tracings within the pulmonary artery or vein were then obtained at ventilatory pressures ranging from 0 to 5, 0 to 10, and 0 to 20 mm. Hg (Fig. 2). The immediate effect of such a ventilatory pressure was recorded and recordings repeated 1, 2, and 3 minutes

after the institution of such pressure. In some instances, where dampened curves were being obtained during the first three minutes, recordings as late as six minutes after assumption of a specific ventilatory pressure were made. It is significant to note that the pressure within the pulmonary vessels assumed the average significant pressure tracing within the first minute in all instances, with few exceptions. These exceptions consisted of 5 patients in whom a vago-vagal type of reflex with drop of systemic blood pressure and pulse was produced after two or three minutes at a ventilatory pressure of 20 mm. Hg. In 3 of these patients, the underlying disease was mitral stenosis, and in 2, the underlying disease was pulmonary emphysema of hypertrophic type.

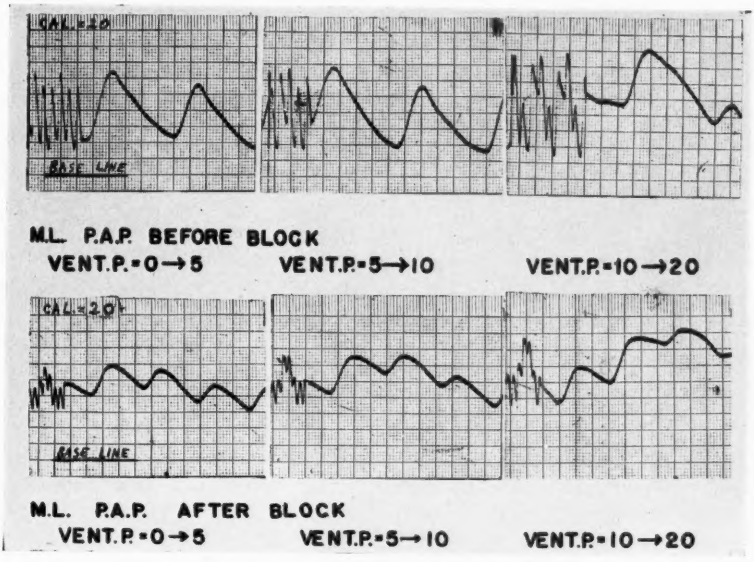

Fig. 2.—Recordings of direct intraluminal pulmonary artery pressures taken at thoracotomy (fast and slow speed of recorder). Tracings at varying ventilatory pressures, demonstrating the parallel rise in pulmonary artery pressure as ventilatory pressure was increased. Block of the vagus nerve with atropine sulfate produced tachycardia, elevation of diastolic produced tachycardia, elevation of diastolic pressure but no change in systolic pulmonary artery pressure. (Patient, M. C., had right middle lobe bronchiectasis; remainder of bronchopulmonary tree appeared normal.)

Following these determinations, the pressure tracings were studied in regard to the effect of various ventilatory pressures in different diseases and the effect of either direct vagus block or pharmacologic block upon such pulmonary vascular pressure responses to varying levels of ventilatory pressure.

During the periods of this study, experience with 6 patients showed us that strikingly abnormal ventilatory pressures may, in themselves, produce a vago-vagal type of reflex, even in the presence of a unilateral direct vagus nerve block, or pharmacologic block with intravenous atropine. A reversal of this type of reflex could be obtained by resumption of normal ventilatory pressures alone. This apparently significant observational by-product of the experiment was analyzed.

TYPES OF DISEASE STUDIED

Cardiac catheterization studies involving the conscious patient with the intact chest were carried out upon 18 patients. The types of disease involved in this study are shown in Table I.

TABLE I. TYPES OF DISEASE STUDIED

DISEASE	NUMBER OF PATIENTS
Hemoptysis, unexplained (normal pulmonary function; MBC 160 L./minute)	1
Pure bullous emphysema	1
Mixed bullous and hypertrophic emphysema	2
Hypertrophic emphysema, Class III (bilateral)	10
Hypertrophic emphysema, Class IV (fixed)	4
Total	18

MBC—Maximum breathing capacity.

TABLE II. PULMONARY ARTERY PRESSURE
DISEASES STUDIED WITH OPEN CHEST

DISEASE	NUMBER OF PATIENTS
Misc. cardiovascular disease	8
Granulomas	3
Primary pulmonary carcinoma	3
Bronchiectasis	4
Pulmonary emphysema	
Bullous	1
Mixed	1
Class III	9
Total	29

Direct pulmonary artery pressure measurements were carried out upon 29 patients. The types of disease involved in this study are shown in Table II. To date there have been 7 direct pressure measurement studies upon the pulmonary vein, and the types of disease so far involved in this method of investigation are designated in Table III.

TABLE III. PULMONARY VEIN PRESSURES
DISEASES STUDIED WITH OPEN CHEST

DISEASE	NUMBER OF PATIENTS
Bronchiectasis	2
Granuloma	1
Granuloma and emphysema	1
Emphysema	2
Mitral stenosis	1
Total	7

EXPERIMENTAL DATA AND RESULTS

Inasmuch as a rather impressive number of figures are obtained with 4 to 6 different pressure studies in the individual patient, it was thought advisable to present a combination of tables. In each instance, therefore, the initial table shows the specific data with the actual recordings for each patient, and a subtable is then presented, outlining the fundamental type of response demonstrated in each patient group at rest or with stress (exercise or high ventilatory pressure), prior to the use of a blocking agent and similar studies thereafter.

Cardiac Catheter Studies (Patient Conscious; Chest Wall Intact).—A total of 18 patients were investigated by means of cardiac catheterization. Right ventricular and pulmonary artery pressures were obtained at rest and during exercise both before and after intravenous administration of a vagus nerve blocking agent, either in the form of 30 mg. of Pro-Banthine or 0.65 mg. of atropine sulfate. The specific data and the summary of the basic changes noted are presented in Tables IVA and IVB. In one instance, a patient who had had a single episode of hemoptysis of unexplained etiology underwent this form of catheter study. Upon x-ray, bronchoscopic, and pulmonary function studies,

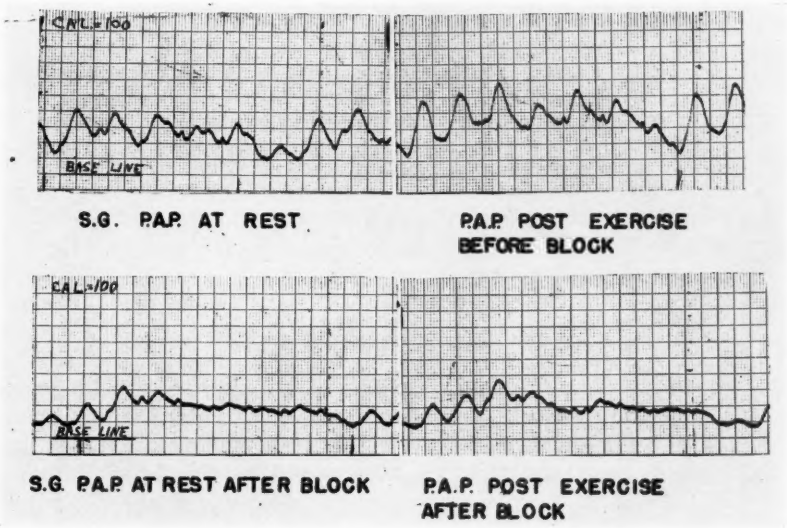

Fig. 3.—Intraluminal pulmonary artery pressure readings obtained at cardiac catheterization showing decrease in pulmonary artery pressure and absence of marked increase after atropine block in a patient with Class III emphysema.

no abnormalities were noted. He was found to have a maximum breathing capacity of 160 L. per minute and we have taken the liberty of considering him as having an essentially normal pulmonary vascular bed. The slight elevation in pulmonary artery pressure is thought to be explained by the mild systolic elevation in systemic blood pressure and a certain amount of anxiety present at the time of the procedure. It is noted that essentially normal systolic and diastolic pressures are recorded at rest with little, if any, change after exercise. After administration of a blocking agent, there is no significant change in the systolic pulmonary artery pressure, but there is a distinct increase in the diastolic component. In the one patient with pure bullous emphysema, which consisted of a well-localized right upper lobe bulla (the remainder of the right lung appeared healthy at operation; there was x-ray evidence of good pulmonary health on the left), the findings were not dissimilar. It should be mentioned that no significant limitation of maximum breathing capacity or other abnormality on standard respiratory function tests were found upon this patient. As soon as

TABLE IVA. CARDIAC CATHETER STUDIES (INTACT CHEST)
PULMONARY EMPHYSEMA; BULLOUS, MIXED BULLOUS AND CLASS III
GROUP I. NO PREVIOUS OPERATION

PATIENT	TYPE	AGE	BLOOD PRESSURE	DRUG	PRESSURES BEFORE DRUG			PRESSURES AFTER DRUG			OTHER EFFECTS		COMMENT
					P.A.-REST	P.A.-EXER.	R.V.	P.A.-REST	P.A.-EXER.	R.V.	O_2 UPTAKE	M.B.C.	
D. S.*	Normal	30	140/90	Atropine	28/17	25/12	--	28/22	27/20	22/5	None	140-60 L./min.	
H. H.	Bullous	46	130/80	Pro-Banthine	22/12	31/15	--	25/12	33/15	37/4	--	160 L./min.	No effect
J. M.	Mixed Bullous	49	124/84	Atropine	25/10	38/17	34/2	25/15	42/27	23/8	--	+35%	No effect
H. G.	Mixed Bullous	45	120/80	Atropine	20/10	37/25	--	30/20	37/26	25/0	None	None	Decrease Rise after exercise
G. S.	Class III	50	130/80	Atropine	36/18	50/27	25/2	25/13	29/15	17/0	--	%	Constant drop
S. W.	Class III		116/70	Pro-Banthine	31/20	65/45	--	37/25	37/25	--	+40%	--	Blocked PAP Rise on exercise
A. C.	Class III		85/65	Atropine	60/37	75/60	55/6	35/25	50/37	35/10	+40%	--	Constant drop
T. W.†	Class III	41	142/100	Pro-Banthine	40/19	45/23	--	39/19	45/30	40/30	--	None	No effect
J. S.‡	Class III	48	115/65	Atropine	25/14	50/20	29/0	25/12	36/20	25/0	--	--	Blocked PAP Rise on exercise

PA=pulmonary artery
RV=right ventricle
PAP=pulmonary artery pressure
*Patient with normal pulmonary function (unexplained hemoptysis).
†Associated major bronchiectasis.
‡Granuloma.

TABLE 1VB. CARDIAC CATHETER STUDIES; EFFECT OF BLOCKING AGENTS ON PULMONARY ARTERY PRESSURE
NORMAL—BULLOUS, MIXED, HYPERTROPHIC PULMONARY EMPHYSEMA (III)
GROUP I. NO PREVIOUS OPERATION

DISEASE OR TYPE	NUMBER OF PATIENTS	AGENT	PREBLOCK		POSTBLOCK	
			REST	EXERCISE	REST	EXERCISE
Normal (?)	1	Atropine	Normal	Normal	Constant diastolic	
Bullous	1	Pro-Banthine	Normal	−45%	Normal	−28%
Mixed	2	Atropine	Normal	−85% −55%	Normal	−23% −68%
III	2	Pro-Banthine	High systolic and diastolic with exercise		Systolic rise depressed Diastolic rise lost	
III	2	Atropine	High systolic and diastolic with exercise		Systolic rise blocked Diastolic rise blocked	
III plus bronchiectasis	1	Atropine	High	−13%	Diastolic raised further	

one goes over into the group of patients having either (a) mixed bullous and true hypertrophic emphysema (Fig. 3) or (b) the diffuse bilateral hypertrophic emphysema with major constant disability but not in a fixed stage (which we have taken the liberty of comparing with the Class III disability noted in cardiac patients), one immediately notes a different response to blocking agents (Fig. 4). Pressures which may be normal at rest rise significantly after exercise before block, and this abnormal rise after exercise is completely eradicated after the use of a blocking agent, or is markedly depressed. We were particularly impressed with the constancy with which the diastolic component tended to drop after use of a blocking agent, in patients with hypertrophic emphysema of a severity comparable to Class III. In contrast to this group of patients, the patients with Class IV emphysema, often referred to as "fixed" in type, showed essentially a constant elevation of pulmonary artery pressure at rest, and often a very dramatic rise with exercise. There was little tendency for the blocking agent to eradicate the systolic rise after exercise, but a definite trend toward prevention of the postexercise diastolic rise was noted. We would like to clarify our definition of a "fixed" pulmonary emphysema patient as one in whom the disease is essentially uniform and diffuse bilaterally, with less than 2 cm. movement of either diaphragm; maximum breathing capacity is always 40 L. per minute or less and is not significantly benefited by any bronchodilating drug. This group of patients did present one definite difference in their response to exercise after drug, when the time for return of the elevated pulmonary artery pressure to the resting base line was estimated. The results of this study are presented in Tables VA and VB. This group consists of 7 patients, who had either true Class IV emphysemas, or emphysema bordering between a low Class III and a high Class IV. An elevation of pulmonary artery pressure was noted at rest and a markedly abnormal elevation to higher limits was noted on exercise. In these patients, blocking agents often decreased the elevation of pulmonary artery pressure at rest down to normal limits, decreased the degree of diastolic rise after exercise, and often considerably depressed the rise in systolic pressure after exercise. The increased speed of return of the pressure levels to the resting base line after completion of exercise was recorded both in minutes and

TABLE VA. CARDIAC CATHETER STUDIES (INTACT CHEST)
PULMONARY EMPHYSEMA (HYPERTROPHIC)—CLASS IV (FIXED)

PATIENT	AGE	BLOOD PRESSURE	DRUG	PRESSURES BEFORE DRUG			PRESSURES AFTER DRUG			OTHER EFFECTS		COMMENT
				P.A.-REST	P.A.-EXER.	R.V.	P.A.-REST	P.A.-EXER.	R.V.	O_2 UPTAKE	M.B.C.	
M. L.	60	98/70	Pro-Banthine	37/25	52/40	—	35/25	55/45	—	None	None	No effect
H. D.	39	95/65	Atropine	47/32	75/57	32/12	38/25	80/70	25/2	None	None	No effect
M. B.*	44	95/70	Atropine	49/30	75/55	42/10	45/12	82/62	42/2	None	None	No effect
C. S.†	39	100/70	Atropine	38/20	50/38	33/12	32/17	52/39	29/8	None	None	No effect

*Silicosis.
†Asthma—bronchiectasis.

TABLE VB. CARDIAC CATHETER STUDIES (INTACT CHEST)
PULMONARY EMPHYSEMA (HYPERTROPHIC)—CLASS IV (FIXED)

NUMBER OF PATIENTS	BLOCKING AGENTS	PRESSURE (REST)	PRESSURE (EXERCISE)	EFFECT
1	Pro-Banthine	High	Higher	None
3	Atropine	High	Higher	None

TABLE VI. EFFECT OF ATROPINE UPON SPEED OF RETURN TO BASE LINE OF ELEVATED PULMONARY ARTERY PRESSURE—POSTEXERCISE (PULMONARY EMPHYSEMA)

PATIENT	TYPE	DIFF. REST	DIFF. EXERCISE	TIME RETURN	PER CENT SPEED RETURN
H. D.	IV	− 9	−20	5 sec. less	50
M. B.	IV	−14	+ 7	9 sec. less	63
C. S.	IV	− 6	+ 2	1 sec. less	16
A. C.	III	−25	−25	3 sec. less	53
A. J.	III	−10	−12	5 sec. less	71
J. S.	III	0	−14	3 sec. less	60
H. G.	Bullous	+10	0	1 sec. less	25
Average		−8 mm. Hg	−10 mm. Hg	−4 Min.	+47%

in the percentage of increased rapidity of return. Figures quite definitely demonstrate an average increased speed of return of approximately 43 per cent faster recovery after administration of blocking agents (Table VI).

A small group of patients were studied who had undergone previous surgery directed toward the pulmonary autonomic nervous system. The results of

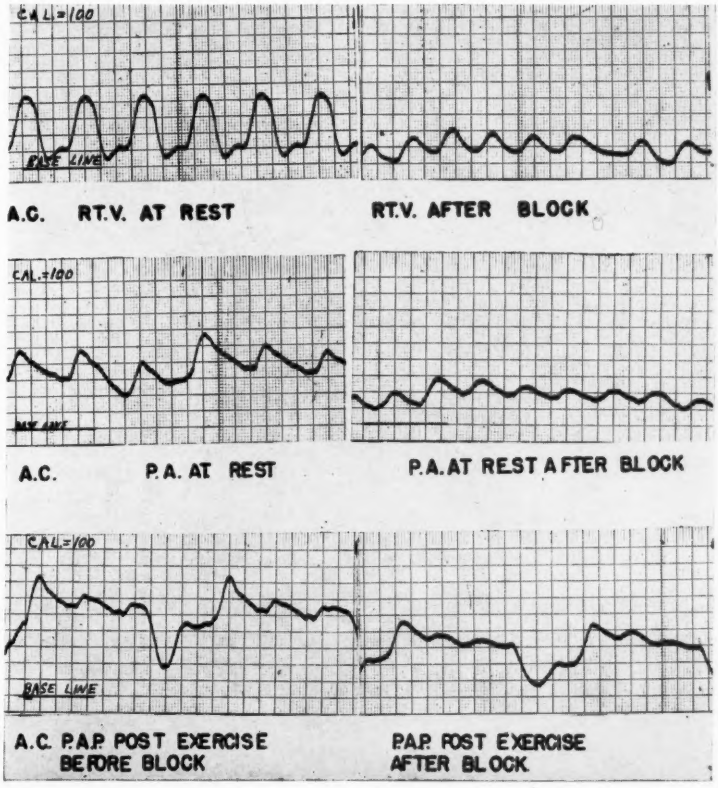

Fig. 4.—Intraluminal pressure recordings obtained at cardiac catheterization in a patient with Class III pulmonary emphysema. This series shows: (1) decrease in right ventricular pressure, and (2) decrease in pulmonary artery pressure at rest and after exercise, produced by intravenous injection of atropine sulfate.

TABLE VIIA. CARDIAC CATHETER STUDIES (INTACT CHEST) PULMONARY EMPHYSEMA (HYPERTROPHIC TYPE)—CLASS III
GROUP II—PREVIOUS DENERVATION

PATIENT	AGE	BLOOD PRESSURE	OPERATION	DRUG	PRESSURES BEFORE DRUG			PRESSURES AFTER DRUG			OTHER EFFECTS		COMMENT
					P.A.-REST	P.A.-EXER.	R.V.	P.A.-REST	P.A.-EXER.	R.V.	O_2 UPTAKE	M.B.C.	
A. J.	38	100/64	Bilateral sympathectomy	Atropine	35/10	52/25	—	25/12	40/29	—	—	+33 per cent	Constant drop
P. A.	50		Bilateral sympathectomy Right vagectomy	Pro-Banthine	26/7	38/15	—	28/18	31/19	—	—	+16 per cent	Pulmonary artery block rise post-exercise
CCR	59	138/95	Left vagectomy	Pro-Banthine	37/12	85/55	44/2	42/22	70/50	48/2	+15 per cent*	20 per cent	Pulmonary artery block rise post-exercise
H. M.	31	110/80	Right vagectomy	—	19/12	23/13	18/3	—	—	—	—	—	Miminal rise post-exercise

*Increased O_2 uptake; +25 per cent right lung, 0 per cent left lung.

TABLE VIIB. CARDIAC CATHETER STUDIES (INTACT CHEST)
PULMONARY EMPHYSEMA (HYPERTROPHIC)—CLASS III
GROUP II—PREVIOUS DENERVATION

NUMBER OF PATIENTS	OPERATION	BLOCKING AGENT	PRESSURE PREBLOCK		PRESSURE POSTBLOCK	
			REST	EXERCISE	REST	EXERCISE
1	Bilateral sympathectomy	Atropine	High	−50 per cent	Normal	−14 per cent
1	Bilateral sympathectomy Unilateral vagotomy	Pro-Banthine	Normal	−45 per cent	Normal	−10 per cent
1	Unilateral vagotomy	Pro-Banthine	High	−125 per cent	High	−75 per cent
1	Unilateral vagotomy	No block	Normal	Normal	—	—

this study are noted in Tables VIIA and VIIB. The number of patients so studied is too limited to permit the drawing of final conclusions at this time but one is quite impressed with the classical Class III type of emphysematous response in the patient who had had bilateral upper dorsal sympathectomy from the level of the first through the sixth dorsal vertebra (Fig. 5). The absence of sympathetic innervation of the lung in the presence of diffuse pulmonary emphysema still permitted a resting pulmonary artery pressure of a distinctly elevated type, with a significant rise after exercise. Pharmacologic blocking of the vagus nerve components to the lung decreased the postexercise systolic and diastolic rise to a significant degree. A somewhat similar response is noted in the patient who had had a bilateral upper dorsal sympathectomy (the first through the seventh dorsal vertebra), with an associated unilateral pulmonary vagectomy. In the 2 patients with unilateral vagectomy instituted on the side of more intense hyper-

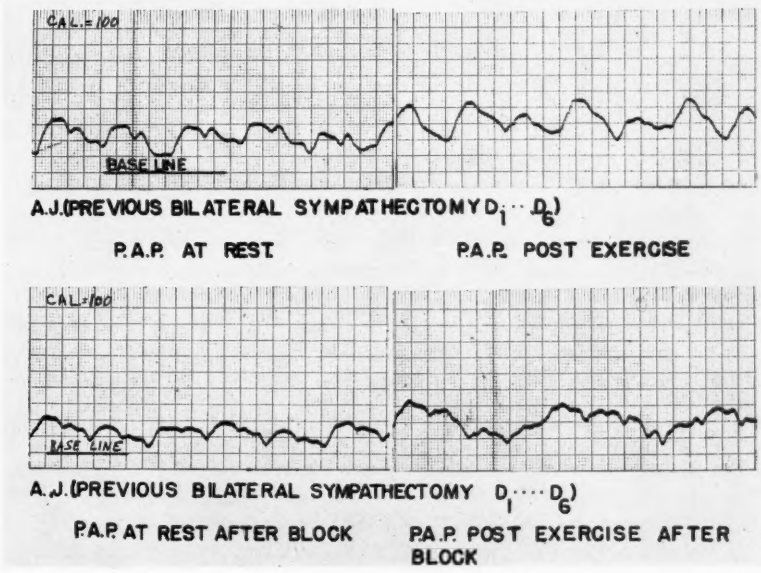

Fig. 5.—Pulmonary artery pressure tracings at cardiac catheterization in a patient with Class III emphysema. She had previously had a bilateral dorsal sympathectomy (D–1 through D–6). Note pulmonary artery hypertension at rest and increase by exercise. Following atropine, pulmonary hypertension was relieved and postexercise rise was decreased.

trophic emphysematous disease, the findings suggest that this is probably a more physiologic approach to the disease entity under question. This type of preoperative catheter study has become a standard procedure in the surgical management of emphysema in this Clinic for the past year and we have abandoned all forms of dorsal sympathectomy as a component of operative procedures for emphysema. It is hoped that a sufficient number of patients will permit postoperative catheterization studies to allow more objective definitive conclusions relative to surgical procedures in this disease.

TABLE VIIIA. PULMONARY ARTERY DIRECT PRESSURE MEASUREMENTS (OPEN CHEST)
MISCELLANEOUS CARDIOVASCULAR LESIONS

PATIENT	AGE	BLOOD PRESSURE	DIAGNOSIS	TYPE OF BLOCK	CHANGES IN PULMONARY ARTERY PRESSURES										COMMENT
					VENT.	P.	5	VENT.	P.	10	VENT.	P.	15	OR 20	
W. C.	17	120/80	Tetrad	Direct	--	—	—	10/5	—	17/10	14/10	—	23/14	(20)	Increased PAP after block
L. S.	29	200/130	Coarctation	Direct	17/4	—	17/4	22/10	—	18/5	25/12	—	21/7	(15)	Fall in diastolic after block
H. A.	24	155/120	Coarctation	Direct	22/12	—	25/16	24/12	—	24/12	27/15	—	24/14	(15)	Fall in diastolic after block
L. L. A.	5	88/70	Patent ductus arteriosus	Direct	27/22	—	28/19	28/21	—	—	26/21	—	33/22	(15)	Elevated PAP higher after block
W. D.	19	110/80	Patent ductus arteriosus	Direct	12/4	—	—	12/6	—	—	19/13	—	20/15	(20)	PAP normal
C. E.	55	144/110	RHD aortic stenosis; mitral insufficiency	Direct	22/18	—	22/18	22/18	—	25/22	24/20	—	25/22	(20)	No change
M. A.	35	108/80	Mitral stenosis	Direct	50/15	—	67/25	52/15	—	48/25	55/23	—	54/32	(20)	Rise in diastolic after block
J. H.	24	118/82	Mitral stenosis	Direct	40/24	—	43/24	43/24	—	43/24	41/24	—	43/26		No change

Vent. P.—ventilatory pressures.
RHD.—rheumatic heart disease.

Direct Pulmonary Artery Pressure Measurements (at Thoracotomy; Open Chest Wall).—

This method of study involving direct pressure measurements, both of the pulmonary artery and of the pulmonary vein, includes a considerably more diversified group of disease entities than the so-called indirect or cardiac catheterization studies. It should be emphasized that the investigative studies were obtained prior to any handling of the lung, opening of the pericardium, or other definitive surgery.

TABLE VIIIB. EFFECT OF VAGUS BLOCK ON PULMONARY ARTERY PRESSURES
DIRECT MEASUREMENT—OPEN CHEST
CARDIOVASCULAR LESIONS

NUMBER OF PATIENTS	DISEASE	METHOD OF BLOCK	EFFECT
1	Tetrad	Direct	Increase after block
2	Coarctations	Direct	Fall in diastolic
2	Patent ductus arteriosus	Direct	Further increase if elevated
1	Aortic stenosis and mitral insufficiency	Direct	None
2	Mitral stenosis	Direct	Rise in diastolic in one; none in other

a. Findings in Miscellaneous Cardiovascular Disease.—The data obtained in the study of various types of patients undergoing thoracotomy for various types of cardiovascular lesions are noted in Tables VIIIA and VIIIB. Only one tracing was recorded in the tetralogy of Fallot group, since there was a tendency throughout this study to confine our studies to the adult patients. In this one instance, it does appear that a significant increase in pulmonary artery pressure, both systolic and diastolic, was recorded after institution of left vagus nerve block. It is interesting to speculate upon the possible comparative benefit from such a block and the improved oxygenation often noted in this patient group after administration of morphine sulfate or Demerol. In the 2 patients with coarctation of the aorta, the pulmonary artery pressure was found to be relatively low in proportion to the systemic blood pressure throughout the entire study. A fall in diastolic pressure with the ventilatory pressure at either 10 or 15 is seen to occur after block in both patients. Two patients with patent ductus arteriosus were examined, and in 1, where the pulmonary artery pressures were within normal limits prior to block, a similar condition persisted after block. In the other patient, in whom a pulmonary hypertension was found throughout the preblock studies, a further increase in the systolic pressure at high ventilatory pressures following direct vagus nerve block was manifested. One patient who had a hiatus hernia, for which surgery was performed, and who had moderately severe associated rheumatic heart disease with aortic stenosis and mitral insufficiency components, showed no significant changes throughout the study. It is interesting to note that in this instance essentially normal pulmonary artery pressures were recorded throughout the study. In 2 patients with Class III mitral stenosis, undergoing mitral commissurotomy, a significant degree of pulmonary hypertension was present at all ventilatory pressures, both before and after direct vagus nerve block. Although no change was noted in

TABLE IXA. PULMONARY ARTERY DIRECT PRESSURE MEASUREMENT (OPEN CHEST)
GRANULOMATOUS LESIONS

PATIENT	AGE	BLOOD PRESSURE	DISEASE	ASSOCIATED PULMONARY DISEASE	TYPE OF BLOCK	CHANGES IN PULMONARY ARTERY PRESSURE									COMMENT
						VENT.	P.	5	VENT.	P.	10	VENT.	P.	20	
A. E.*	45	160/100	Granuloma	Segmental emphysema	Atropine	20/0	→	16/0	22/2	→	18/4	27/16	→	23/9	Drop in PAP after block
W. T. M.	50	144/86	Granuloma	Segmental emphysema RUL—RML	Atropine	16/5	→	17/7	16/5	→	17/7	26/15	→	21/14	Drop in PAP after block at 20
M. Y.	42	100/70	Asbestosis granuloma	None	Atropine	14/5	→	14/8	18/8	→	19/12	20/9	→	22/15	Rise in diastolic

*Associated segmental areas hypertrophic emphysema.

TABLE IXB. EFFECT OF VAGUS BLOCK ON PAP
DIRECT MEASUREMENT—OPEN CHEST
GRANULOMATOUS LESIONS

NUMBER OF PATIENTS	ASSOCIATED DISEASE	METHOD OF BLOCK	EFFECT
1	None	Atropine	Rise in diastolic
2	Emphysema	Atropine	Drop at 20 in both Drop at 5 and 10 in one

one of these patients, in the other patient a constant trend toward a higher diastolic pressure at all ventilatory pressures was recorded after institution of vagus nerve block. It is not felt that a sufficient number of patients of each type is included in this study group to make any definitive impressions. However, there are certainly interesting differences in the pre- and postblock pressure measurements in the 5 types of cardiovascular lesions indicated. It would appear that a disease which is characterized by high resting pulmonary artery pressure such as patent ductus arteriosus and mitral stenosis shows no tendency toward decrease in the systolic pressure after block, while the diastolic pressure may increase. The apparently significant rise in pulmonary artery pressure after vagus nerve block in the single patient studied with pulmonary hypotension is of interest.

b. Granulomatous Lesions.—Studies were carried out upon 3 patients undergoing thoracotomy for peripheral granulomas. In 2 of these patients, distinct areas of emphysematous change in the basilar segments of the lower lobe and the medial segment of the middle lobe were found to be present. Details of this study are shown in Table IXA, with the summary of the basic changes produced portrayed in Table IXB. The patient with some asbestosis and a solitary peripheral granuloma and no emphysema presented essentially the findings expected to be seen in the normal lung. Specifically, a progressive increase in systolic pressure was noted with increased ventilatory pressure, with a slight concomitant rise in diastolic pressure at these levels. The major change produced by intravenous atropine was again a rise in the diastolic pressure. In 2 patients with granulomas having associated emphysema, the typical emphysema response (a drop in systolic and diastolic pressures at high ventilatory pressure levels) was noted after administration of the blocking agent.

c. Primary Pulmonary Carcinoma.—Tables XA and XB record the findings in a group of 3 patients undergoing thoracotomy for peripherally placed primary pulmonary carcinoma. In two instances when the remainder of the lung tissue appeared normal, an essentially normal study was obtained, with progressive rise in systolic and diastolic readings, paralleling increases in ventilatory pressures prior to administration of blocking procedures, while after block there appeared to be a major rise in diastolic pressure and a tendency to increase in the systolic pressure. In the third patient, 72 years of age, with considerable arteriosclerosis and diffuse emphysema, a more classical emphysema type of recording was obtained.

d. Bronchiectasis.—(Tables XIA and XIB.) A group of 4 patients undergoing resectional procedures for bronchiectasis were studied by direct pulmonary artery pressure measurements. In 3 of these patients, a remarkably static group of figures was obtained, showing essentially no significant effect of the block except possibly for the lack of the expected rise in diastolic pressure noted in the normal response to atropine or vagus block. The fourth patient in this group, who had advanced bilateral bronchiectasis and who had previously had the right middle and right lower lobes removed, was found at the time of left-side resectional surgery to have a very significant degree of pulmonary hypertension. The findings both before and after block suggest a very fixed type

TABLE XA. PULMONARY ARTERY DIRECT PRESSURE MEASUREMENTS (OPEN CHEST)
PRIMARY PULMONARY CARCINOMA

PATIENT	AGE	BLOOD PRESSURE	ASSOCIATED PULMONARY DISEASE	TUMOR SITE	TYPE OF BLOCK	CHANGES IN PULMONARY ARTERY PRESSURE						COMMENT
						VENT. P. 5		VENT. P. 10		VENT. P. 20		
J. C.	52	104/80	None	LUL	Direct vagus	11/8	10/6	16/6	16/10	24/10	32/24	Rise after block at 20
H. S.	52	120/80	None	Apex of LUL	Atropine	15/0	17/0	15/2	23/5	27/9	37/20	Rise after block at 20
W. R.	72	170/100	Arteriosclerosis and emphysema	LUL	Atropine	27/6	14/3	26/8	17/5	33/17	31/16	Drop after block

TABLE XB. EFFECT OF VAGUS BLOCK ON PAP
DIRECT MEASUREMENT—OPEN CHEST
PRIMARY PULMONARY CARCINOMA

NUMBER OF PATIENTS	ASSOCIATED DISEASE	METHOD OF BLOCK	EFFECT
1	None	Direct	Rise after block at 20
1	None	Atropine	Rise after block at 20
1	None	Atropine	Constant drop after block

TABLE XIA. PULMONARY ARTERY DIRECT PRESSURE (OPEN CHEST)
BRONCHIECTASIS

PATIENT	AGE	BLOOD PRESSURE	LOCATION OF DISEASE	TYPE OF BLOCK	CHANGES IN PULMONARY ARTERY PRESSURE						COMMENT
					VENT. P. 5		VENT. P. 10		VENT. P. 20		
T. H.	25	132/94	L.L. lobe and lingula Right M. and L. lobes removed previously	Direct vagus block	43/23	43/25	40/22	43/30	45/28	43/33	High basal PAP diastolic rise at 10 and 20
V. R.	29	115/80	Right middle and lower lobes	Direct vagus	17/7	18/8	17/7	19/8	22/12	22/12	No significant change
M. L.	47	110/80	Right middle lobe	Atropine	15/5	15/11*	18/7	16/12*	22/13	19/12	*Parallels rise in systemic pressure
J. N.	26	105/70	Left lower lobe	Direct vagus	13/7	14/8	--	--	17/14	18/14	No significant change

*Associated hypertrophic type emphysema noted in basilar segments.

TABLE XIB. EFFECT OF VAGUS BLOCK ON PULMONARY ARTERY PRESSURE
DIRECT MEASUREMENT—OPEN CHEST
BRONCHIECTASIS

NUMBER OF PATIENTS	ASSOCIATED DISEASE	METHOD OF BLOCK	EFFECT
2	None	Direct	None
1	None	Atropine	None
1	Pulmonary hypertension	Direct	Diastolic rise at Vent. P. 10 + 20

TABLE XIIA. PULMONARY ARTERY DIRECT PRESSURE MEASUREMENT (OPEN CHEST)
PULMONARY EMPHYSEMA

PATIENT	AGE	BLOOD PRESSURE	CLASS	ASSOCIATED DISEASE	TYPE OF BLOCK	CHANGES IN PULMONARY ARTERY PRESSURE						COMMENT
						VENT. P. 5		VENT. P. 10		VENT. P. 20		
J. S.	48	115/65	III	None	Atropine	--	--	15/2	14/3	19/7	16/6	Drop after block
H. G.	45	120/80	Bullous	None	Vagotomy	--	--	--	--	22/11	21/8	No change
H. H.	42	136/90	Bullous mixed	None	Direct vagus	14/10	6/3	10/6	6/2	18/12	14/7	Drop after block
N. T.	48	170/120	III	Bronchiectasis RML	Direct vagus	25/9	18/8	22/8	16/10	29/15	26/15	Drop after block
J. M.	53	130/90	III*	None	Direct vagus	14/3	13/2	18/7	16/5	26/11	26/17	Systolic BP rose 40 mm./Hg during recordings
H. M.	44	120/90	III	None	Atropine	--	--	20/6	23/5.9	46.3/38	42.8/28	Systolic BP rose 15 mm./Hg during recordings
T. W.	44	142/100	III	Bronchiectasis	Direct vagus	20/11	15/6	22/10	15/7	27/13	19/10	Drop after block
J. R.	60	140/100	III	None	Direct vagus	15/7	12/7	17/8	13/7	21/10	15/6	Drop after block
W. R.	72	170/100	III	Bronchogenic carcinoma	Atropine	27/6	14/3	26/8	17/5	33/17	31/16	Drop after block
A. E.	45	160/100	III	Granuloma	Atropine	20/0	16/0	22/2	18/4	27/16	23/9	Drop after block
W. T. M.	50	144/86	III	Granuloma	Atropine	16/5	17/7	16/5	17/7	26/15	21/14	Drop after block at 20

*Large apical bulla with severe hypertrophic emphysema, rest of lung.

of pulmonary resistance with little change in the systolic pressure response to changes in ventilatory pressure and a suggestive significant rise in diastolic pressure when the ventilation reading was 10 and 20.

e. Pulmonary Emphysema.—Tables XIIA and XIIB designate the findings of direct pulmonary artery pressure studies on patients with different types of pulmonary emphysema. Again, one should mention that these patients had had preoperative cardiac catheterization studies. The details of comparison of these two methods of study of the same patient will be presented in a later communication. At the present time, our evidence indicates that there is a distinct parallel between the findings by the two methods. Pulmonary artery pressures tend to be distinctly lower in the lateral decubitus position under anesthesia than they are in the supine position in the conscious state.

TABLE XIIB. EFFECT OF VAGUS BLOCK ON PAP
DIRECT MEASUREMENT—OPEN CHEST
PULMONARY EMPHYSEMA

TYPE	NUMBER	METHOD OF BLOCK	NO EFFECT	DROP ONLY AT 20	CONSTANT DROP
Bullous	1	Direct	1	–	–
Mixed	1	Direct	–	–	1
III	4	Direct	–	–	4
III	5	Atropine	–	3	2

In the patient with pure bullous emphysema, a slight drop in diastolic pressure at high ventilatory pressures was noted after block. In the 1 patient with mixed bullous and hypertrophic emphysema, a distinct tendency toward a drop in pressure after block was noted at all ventilatory pressure levels. In the third patient undergoing surgery for a large apical bulla, but in whom an extreme degree of diffuse hypertrophic emphysema was present, the vagus block produced a relative drop in systolic pressure at all ventilatory pressure levels. Following direct vagus block, the patient's systemic blood pressure increased 40 mm. Hg, and yet the pulmonary artery pressures after block were no higher than those taken prior to physiologic denervation. In the remaining 8 patients with Class III hypertrophic emphysema undergoing surgery consisting of resection of localized bronchiectasis plus vagotomy, lobectomy for carcinoma, subsegmental resection for granuloma, or vagectomy for hypertrophic emphysema, there was a marked similarity of response. It would suggest that there is a classical pattern in hypertrophic emphysema such that, following atropine or direct vagus nerve block, the pulmonary artery pressure (both systolic and diastolic) shows a significant fall at most ventilatory pressure levels.

Effect of Vagus Block on Pulmonary Vein Pressure Using Direct Measurement Technique.—

To date, 7 patients have undergone either isolated pulmonary vein studies or concomitant pulmonary vein and pulmonary artery pressure measurements. The findings in 7 patients, including various types of lesions, are presented in Tables XIIIA and XIIIB. These early findings would suggest that little significant effect is obtained in such diseases as bronchiectasis, granuloma, or mitral stenosis, but a constant decrease in pulmonary venous pressure after block may occur in hypertrophic emphysema. The need for further concomi-

TABLE XIIIA. PULMONARY VEIN PRESSURE MEASUREMENTS (OPEN CHEST)

PATIENT	AGE	BLOOD PRESSURE	DISEASE	POSITION	TYPE OF BLOCK	CHANGE IN PULMONARY VEIN PRESSURES						COMMENT
						VENT. P. 5		VENT. P. 10		VENT. P. 20		
D. C.	22	130/95	Right M. and L. lobe bronchiectasis	Face down	Atropine sulfate	14/7	15/4	17/10	16/8	21/18	24/4	No significant effect
G. R.	26	108/70	Right M. lobe bronchiectasis	Anterolateral	Direct vagus	8/3	12/8	8/6	12/10	13/9	12/9	Increased P at 5 and 10 after block
A. K.	34	98/60 80/62	Mitral stenosis	Anterolateral	Direct vagus	--	--	17/10	18/14	23/15	27/20	Some increase at 20 after block
H. G.	45	120/80	Emphysema	Lateral	Vagotomy	+1/-3	-2/-8	+2/-3	0/-4	10/5	6/2	Decreased PVP after block
J. S.	48	160/110	Emphysema	Lateral	Atropine	+1/-2	-5/-10	-1/-5	-2.5/-7.5	1.5/-1.5	0/-5	Decreased PVP after block
E. T.	50	100/80	Left lower lobe granuloma	Lateral	Direct vagus	9/4	13/6	12/7	9/5	16/9	14/9	No significant change
W. K. P.	27	106/80	Granuloma and basilar segment emphysema	Lateral	Direct vagus	3/-2	3/-2	3/0	4/1	7/3	14/10	Increase at 20 after block

PVP—pulmonary vein pressures.

TABLE XIIIB. EFFECT OF VAGUS BLOCK ON PULMONARY VEIN PRESSURE
DIRECT MEASUREMENT—OPEN CHEST
MISCELLANEOUS DISEASES

NUMBER OF PATIENTS	DISEASE	METHOD OF BLOCK	EFFECT
1	Bronchiectasis	Atropine	None
1	Bronchiectasis	Direct	None
1	Granuloma	Direct	None
1	Granuloma and emphysema	Direct	None except increase at 20
1	Emphysema	Direct	Constant decrease
1	Emphysema	Atropine	Constant decrease
1	Mitral stenosis	Direct	None except increase at 20

tant pulmonary artery and vein direct pressure measurements is emphasized by this early pilot study. Concomitant studies in our respiratory function laboratory show an essentially constant major increase in oxygen uptake by emphysematous patients (Class III or above) after administration of such drugs as atropine, aminophylline, Pro-Banthine, Isuprel, and Adrenalin. Certainly much of the detail of the pathologic physiology of pulmonary emphysema is not as yet adequately defined.

Production and Control of Vago-Vagal Type Syndrome by Regulation of Ventilatory Pressure.—

Tables XIVA and XIVB outline a series of events which occurred in 6 patients (5 of whom were in the study group), of a total of 33 patients undergoing direct pressure measurement study. This constituted the single important, essentially dangerous complication of this study. In 3 patients with mitral stenosis, the effect of rise of ventilatory (inspiration) pressure from 10 to 20 mm. Hg upon the blood pressure and pulse was recorded. In 2 of these patients, concomitant pulmonary artery pressure readings were obtained. With the rise of ventilatory pressure to 20, constant drop in blood pressure and slowing of pulse were obtained. Direct vagal block could not alter this course of events but a return to normal status of such vital signs as blood pressure and pulse was obtained by resuming a ventilatory pressure of 10 mm. Hg. An exactly similar situation obtained in 2 patients with pulmonary emphysema undergoing direct pressure measurements. In 1 of these, intravenous atropine failed to block the reflex and, in the other, direct left vagus nerve injection with 1 per cent procaine failed to alter the physiologic disturbance. In both these patients, the resumption of normal pulmonary artery pressure, systemic blood pressure, and pulse obtained upon instituting a more physiologic ventilatory (inspiration) pressure, viz., 10 mm. Hg. In the sixth patient noted on these tables, who was not undergoing ventilatory pressure studies, but undergoing mitral commissurotomy, the precommissurotomy pressure readings in the pulmonary artery and in the left atrium revealed a bizarre disproportion of pressures. The intimation that this marked disproportion indicated a mechanical block to blood flow through the lung was not immediately appreciated and a severe drop in systemic blood pressure and slowing of the pulse ensued. Investigation revealed that the balloon of the endotracheal tube was overdistended and lapping over the end of the endotracheal airway. This was relieved and the operation proceeded. Following a classical commissurotomy, the pulmonary artery pressure dropped to 22/10, while the left auricular pressure decreased to 8/6. It has not been our experience to see a pulmonary artery pressure of 70 decrease to less than 40 or 50 after commissurotomy on readings obtained at the operating table. We, therefore, infer that this patient's precommissurotomy pulmonary artery pressure was probably somewhere in the neighborhood of 30 mm. Hg, systolic, until an obstructed airway intervened. It has long been our contention[24] that manual and mechanical positive pressure, as well as abnormally high ventilatory pressures prior to opening the thorax in patients with obstructive lesions of either the right ventricular outflow tract or the left ventricular inflow tract, is highly deleterious. The evidence presented above would tend to confirm that impression.

TABLE XIVA. PRODUCTION OF VAGO-VAGAL TYPE SYNDROME BY HIGH VENTILATORY PRESSURE. CORRECTION OF SYNDROME BY REDUCING PRESSURE ONLY

PATIENT	AGE	DISEASE	TEST	VENT. P. 10 BP	VENT. P. 10 P	VENT. P. 10 PAP	VENT. P. 20 BP	VENT. P. 20 P	VENT. P. 20 PAP	VENT. P. 10 BP	VENT. P. 10 P	VENT. P. 10 PAP	COMMENTS
W. H.	30	Mitral stenosis	Increase vent. p.	130/90	72	N.R.	112/80	72	N.R.	122/90	72	N.R.	No block
M. A.	35	Mitral stenosis	Increase vent. p.	90/60	100	52/14 → 48/25	70/50	80	55/23 → 54/32	88/60	80/100	48/25	BP unchanged PAP diastolic elevated by left vagus block
A. K.*	34	Mitral stenosis	Increase vent. p.	98/60	120	N.R.	88/60	86	N.R.	98/62	92	N.R.	BP effect unchanged by left vagus block
G. C.	40	Mitral stenosis	Partial respiratory obstruction	--	--	--	Obstruction 90/60 0	↓ 0	70/50	No obstruction 98/60	80	22/10	During obstruction PAP 70/50 LAP 12/5 After obstruction PAP 22/10 LAP 8/6
J. S.†	48	Pulmonary emphysema	Increase vent. p.	160/110	80	15/2	100/60	100	19/7	160/110	120	14/3	Effect unchanged by atropine gr. 1/100
T. W.	44	Pulmonary emphysema	Increase vent. p.	160/100	80	22/10 → 15/7	140/90	60	27/13 → 19/10	160/100	80	20/11 → 15/6	Effect unchanged by direct block left vagus

P.—Pulse.
*With fall in BP, the PVP rose both before and after block.
†With fall in BP, the PVP rose both before and after block.

TABLE XIVB. PRODUCTION OF VAGO-VAGAL TYPE SYNDROME BY HIGH VENTILATORY PRESSURES

NUMBER OF PATIENTS	DISEASE	EFFECT RISE VENT. P. 10 — 20	EFFECT DROP VENT. P. 20 — 10	EFFECT OF BLOCK
3	Mitral stenosis	1. High PAP unchanged 2. Constant BP drop 3. Pulse drop if high or normal	1. High PAP unchanged 2. Constant BP rise 3. Rise in pulse	None
2	Emphysema	1. PAP increased 2. BP dropped 3. Pulse slowed	1. PAP dropped 2. BP rose 3. Pulse speeded	None 1 Atropine 1 Direct
1	Mitral stenosis with respiratory obstruction	With obstruction and stenosis 1. PAP 70/50 LAP 12/5 2. BP severe drop 3. Pulse slow	Obstruction and stenosis relieved 1. PAP 22/10 LAP 8/6 2. BP normal 3. Pulse normal	

SUMMARY AND CONCLUSIONS

We have presented 2 groups of patients studied by different methods relative to the effect of vagus nerve blocking agents upon the pulmonary vascular dynamics in the presence of various cardiovascular and pulmonary diseases. Eighteen patients were studied by cardiac catheterization in the conscious state with the chest wall intact, and physiologic vagus block produced by the use of either intravenous Pro-Banthine or atropine sulfate. In a second group of 33 patients, direct pressure measurements were made upon the pulmonary artery, pulmonary vein, or both, at the time of thoracotomy for various cardiovascular or pulmonary disease states. The statistical data obtained by this method of study have been presented, reviewed, and summarized.

We feel justified in drawing the following conclusions:

1. Studies upon the effect of various drugs which have known specific effects upon the autonomic nervous system, on the pressure tracings obtained from the right heart and pulmonary artery in different cardiovascular and pulmonary diseases as well as in the normal human being should help to clarify our knowledge relative to the control of the heart, great vessels, and lung by the autonomic nervous system.

2. Intravascular pressure tracings obtained at the operating table under standardized conditions of anesthesia and ventilatory pressure constitute a new and useful tool for the investigation of the pathologic physiology of thoracic disease.

3. Such studies at the operating table can apparently be done without hazard to the patient if one is conscious of the capacity of higher ventilatory pressures to produce a vago-vagal type of reflex syndrome.

4. Study of the effect of different drugs or of the application of blocking agents to the sympathetic and parasympathetic nervous system can enhance the value of the direct pressure measurements made at the time of thoracotomy.

5. The pulmonary artery pressure in the patient with a normal cardiovascular-pulmonary state should not rise after exercise, but a rise in diastolic pressure is noted after pharmacologic vagus nerve block, both at rest and after exercise.

6. Essentially similar findings were recorded for a patient with bullous emphysema and another with isolated peripheral granuloma, and in 2 patients with peripheral primary carcinoma in conjunction with normal appearing lung tissue.

7. In patients with mixed bullous and hypertrophic emphysema, and patients with pure hypertrophic emphysema, Class III, the expected rise in pulmonary artery pressure after exercise was markedly depressed or blocked completely after injection of the pharmacologic vagus nerve blocking agent. There was a distinct reduction in diastolic pressure in the pulmonary artery, both before and after exercise in emphysematous patients following institution of such a nerve block.

8. In patients with so-called "fixed" pulmonary emphysema, who had usually progressed to secondary pulmonary vascular changes (producing an irreversible pulmonary resistance) the vagus nerve block did not reduce the postexercise systolic pressure rise, nor was the diastolic pressure in the pulmonary artery depressed.

9. However, in patients with Class IV emphysema, a more rapid return of an elevated postexercise pressure to the resting base line was obtained after the institution of pharmacologic block of the parasympathetic nervous system.

10. Cardiac catheter studies upon a small group of patients having had previous surgery directed toward the pulmonary autonomic nervous system suggest that a harmful effect is obtained from dorsal sympathectomy and a beneficial one from pulmonary vagectomy, in patients with Class III pulmonary emphysema.

11. Direct pulmonary artery pressure measurements upon a group of patients with miscellaneous cardiovascular disease suggest that vagus nerve block increases pulmonary artery pressure in tetralogy of Fallot, that the diastolic pressure may be depressed by higher ventilatory pressures in coarctation of the aorta, while in pre-existent pulmonary hypertension in patent ductus arteriosus this pressure may be further elevated by direct vagus nerve block. The significant pulmonary hypertension noted in patients with mitral stenosis is essentially unaffected in its systolic component by variance in the ventilatory pressure before or after vagus nerve block. However, in this group of patients, the diastolic pressure may increase at various ventilatory pressures after block.

12. Patients with unilateral bronchiectasis demonstrated essentially a normal pattern of pressure measurement pulmonary vascular dynamics before and after vagus nerve block, except that the diastolic pressure tended to show no effect in response to administration of the blocking agents.

One patient with advanced bilateral bronchiectasis and associated pulmonary hypertension showed the findings expected with a fixed type of pulmonary resistance such as is seen with pulmonary arteriosclerosis, pulmonary arteriolar sclerosis, or mitral stenosis. Direct pressure measurement studies on patients with pulmonary emphysema showed little significant change in patients with pure bullous emphysema, but significant change in mixed bullous and hypertrophic or pure hypertrophic emphysema.

13. The drop in systolic and diastolic pressure after atropine at average ventilatory pressures and high ventilatory pressures parallels the findings noted

in study of pulmonary artery pressures at rest and during exercise in conscious patients undergoing cardiac catheterization.

14. Too few studies on pulmonary venous pressure have been carried out to make definitive conclusions, except that the initial pilot study promises that major information can be obtained from concomitant pulmonary artery and vein direct pressure measurements.

15. A vago-vagal type of syndrome with severe drop in systemic blood pressure, slowing of the pulse, and either elevation of the pulmonary artery pressure or maintenance of a high pulmonary artery pressure, if already elevated, can be produced by high ventilatory pressures. This vago-vagal type of syndrome persists despite administration of intravenous atropine or unilateral direct vagus nerve block. The changes are reversible by returning the ventilatory pressure to more physiologic limits.

16. Studies suggest that the pulmonary artery pressure found in health and disease was dependent upon: (a) right ventricular pressure and output, (b) the competence of the pulmonary valve, (c) the tone of the pulmonary arterial wall, both as it may be affected by sclerosis and by spasm secondary to reflex autonomic nervous control, (d) abnormal systemic vascular to pulmonary vascular system shunts, (e) the pressure within the alveolus, and (f) the resistance presented by the inflow tract of the left heart (tone of the pulmonary vein wall, status of left auricle and mitral valve).

17. The vagus nerve appears to have the capacity to increase the pressure within the pulmonary artery by either contracture of the arterial wall, or increasing the pressure within the alveolus by bronchospasm, or both.

18. The capacity of vagal nerve blocking agents to produce: (a) increased ventilatory capacity, (b) decreased pulmonary artery pressure, and (c) concomitant increase in oxygen uptake at rest and during stress in pulmonary emphysema suggests that a pathologic degree of vagotonia is present in this disease.

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DISCUSSION

DR. ELTON WATKINS, JR., Boston, Mass.—I have followed the very interesting work of Dr. Abbott, Dr. Sloan, Dr. William Adams, and others, in the forgotten field of lung circulation in various disease states. The studies are difficult to do and more difficult to interpret. Consequently, I would like to ask Dr. Abbott one question, whether he has drawn any conclusions as to the site of action of these various types of autonomic nerve procedures. The reason I ask this question is that many years ago Dr. William F. Hamilton showed that when he tinkered with the autonomic nervous system in experimental animals, there were changes in pulmonary artery pressure, but these changes resulted from the influence of the autonomic agent upon the systemic vascular bed. As an injected autonomic drug passed through the lungs, very little change in pulmonary artery pressure occurred until the agent hit the peripheral circulation, when vasomotor changes occurred which shifted blood from the pulmonary vascular bed to the systemic vascular bed with a resulting decline in pulmonary artery pressure. The reason I raise the point here is that, if the observed alterations in pulmonary artery pressure are the result of changes in the systemic vascular bed, the reduction of pulmonary artery pressure observed by Dr. Abbott may be accompanied by deleterious peripheral circulatory effects of much greater significance than the pulmonary artery pressure changes.

DR. ABBOTT (Closing).—The question asked as to the exact action of these drugs, of course, is difficult. There is some evidence to indicate that the action is upon neurogenic control of bronchial musculature. I think we should emphasize the fact that the findings following drug action with effect upon the heart in the catheterized patient with the intact chest are similar to unilateral vagotomy, except not quite as complete as the unilateral vagotomy produced by direct injection of the isolated vagus nerve. The persistence of action of these denervations is particularly striking in studying serial studies of patients before and after unilateral vagotomy. The denervated lung which presented major obstruction to air flow on expiration prior to vagotomy expels air approximately twice as fast as the contralateral lung. Thus, on fluoroscopic examination during forced expiration, a shifting of the mediastinum toward the side not operated upon is produced until contralateral vagotomy is performed. This action, therefore, of denervation producing release of obstructive hypertonicity of the bronchial musculature is evident upon fluoroscopic examination. Evidence is also obtained by the bronchoscope of the lack of contractural capacity of the bronchial musculature following pulmonary vagotomy. The fact that investigations with the open chest show that high endobronchial ventilatory pressure produces alterations in pulmonary vascular dynamics only partially affected by denervation suggests to us that the action is motivated as follows: The change in air pressure within the alveolus is a direct result of the tone of entering bronchiole into the atrium musculature plus the endobronchial ventilatory pressure. The effect of this pressure within adjacent alveoli upon the interposed pulmonary vascular bed constitutes a petcock action, and thus, in part, controls the pressure within the pulmonary artery and vein. Indeed, this facet of control of the lesser circulation by variance in intra-alveolar pressure is reflected also into the greater circulation. There is not time available to define the mechanisms existent to effect this intra-alveolar pressure, but one may confidently state that the action of the vagus nerve in this regard is becoming increasingly evident.

TEMPORARY UNILATERAL OCCLUSION OF THE PULMONARY ARTERY IN THE PREOPERATIVE EVALUATION OF THORACIC PATIENTS

A Preliminary Report

Herbert Sloan, M.D., Joe D. Morris, M.D. (by invitation), Melvin Figley, M.D. (by invitation), and Robert Lee, B.S. (Chem.) (by invitation)
Ann Arbor, Mich.

INTRODUCTION

THE ability of a patient with impaired cardiorespiratory function to tolerate pulmonary resection is difficult to evaluate. Satisfactory methods are available for the measurement of pulmonary function and the decrease in ventilatory function, which will result from a pulmonary resection, can be predicted. It is now recognized that inability of the cardiovascular system to compensate for a reduction in the pulmonary vascular bed following pulmonary resection may be as important as a reduction in ventilatory function in determining the outcome of operation. The desirability of studying the cardiovascular system in patients being considered for pulmonary resection has not been emphasized sufficiently despite deaths following operation which were due to pulmonary hypertension.[1, 2]

In 1951, Carlens, Hanson, and Nordenström[3] occluded one pulmonary artery temporarily with an inflatable balloon at the tip of a cardiac catheter. Extensive physiologic and angiographic studies of the pulmonary circulation employing this method were carried out.[4-6] Nemir, Stone, Mackrell, and Hawthorne combined temporary occlusion of a pulmonary artery with occlusion of the bronchus to the same lung.[7-9] These techniques have made it possible to produce the circulatory and ventilatory changes which might be expected to follow pulmonary resection as well as to evaluate the ability of the circulatory system to compensate for a reduction in the pulmonary vascular bed.

Studies of the circulatory changes following temporary unilateral occlusion of the pulmonary artery have been carried out by us in 18 patients being considered for pulmonary resection. Sixteen of the patients had carcinoma of the lung. One patient had bilateral obstructive emphysema due in part to bronchial compression by lymph nodes and the remaining patient had a localized inflammatory lesion.

METHODS

The patient was brought to the catheterization unit without breakfast after sedation with 75 mg. of Demerol. A double lumen Dotter-Lukas catheter

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with a distal occluding balloon and a proximal sampling orifice was passed through the left median basilic vein into the pulmonary artery of the involved lung. The left brachial artery was punctured with a No. 16 needle and a flexible wire stylet was passed through the needle into the artery. The needle was withdrawn and a polyethylene catheter with an inside diameter of 0.047 inch and an outside diameter of 0.067 inch was passed over the stylet into the artery. The stylet was then withdrawn. The end of the catheter was obturated with a No. 18 needle and a stopcock. Arterial samples and pressures were measured through the stopcock. The needle and stopcock were removed during the collection of samples for cardiac output in order to obtain maximum flow through the polyethylene tube.

Measurements of pulmonary artery and brachial artery pressures were made with Statham strain gauges and recorded with a Sanborn Twin Viso-Cardiette. The zero reference level was 10 cm. from the table top. The electrocardiogram was monitored continuously. Cardiac outputs were determined by the dye method after earlier attempts to measure cardiac output by the Fick principle yielded results which were not satisfactory. For each cardiac output, 5 mg. of T-1824 were injected into the pulmonary artery proximal to the balloon through the catheter. Serial arterial samples were collected in tubes rotating on a kymograph. Determinations of dye in the samples were made with a 6-A Coleman Junior Spectrophotometer. Oxygen saturations were determined by the method of Van Slyke and Neill.

Data were collected with the pulmonary artery patent, following unilateral occlusion of the pulmonary artery and during moderate exercise with occlusion of the pulmonary artery. The average duration of pulmonary artery occlusion was forty-five minutes. During each part of the study, the following determinations were made: pulmonary artery and brachial artery pressures, oxygen saturations of pulmonary artery and brachial artery blood, and cardiac output. The right or left pulmonary artery was occluded by the injection of 5 to 7 c.c. of 35 per cent Urokon into the balloon. The balloon was filled under fluoroscopic control until it no longer moved in the pulsating pulmonary arterial stream and it began to conform to the outline of the pulmonary artery. Data were obtained after the balloon had been inflated at least ten minutes. Fifteen to twenty minutes later, while the balloon remained inflated, these data were collected during moderate exercise. The exercise consisted of bicycling against arm resistance. The exercise was continued for seven minutes and the data obtained during the last two minutes of exercise. The position of the inflated balloon was checked fluoroscopically from minute to minute. Maximum breathing capacity, total vital capacity, and one second timed vital capacity were obtained on each patient.

RESULTS

In 18 patients, it was possible to occlude the pulmonary artery of the involved lung and to carry out studies on the systemic and pulmonary circulations. Attempts to occlude the pulmonary artery were unsuccessful in 4 additional patients. The catheter could not be passed into the pulmonary

artery in 2 of these patients. The balloon burst as it was inflated in a third patient. The fourth patient had rectal bleeding from a recent sigmoidoscopy during the catheterization.

Insertion of the catheter and inflation of the balloon were only a little more difficult than manipulation of the catheter in a routine cardiac catheterization. Most of the patients tolerated occlusion of one pulmonary artery well and had no symptoms during the period of occlusion. A few patients were subjectively short of breath, but no patient was dyspneic. One patient noticed that his hearing and vision were more acute after the balloon was deflated, although he had not been aware of any abnormality while the pulmonary artery was occluded.

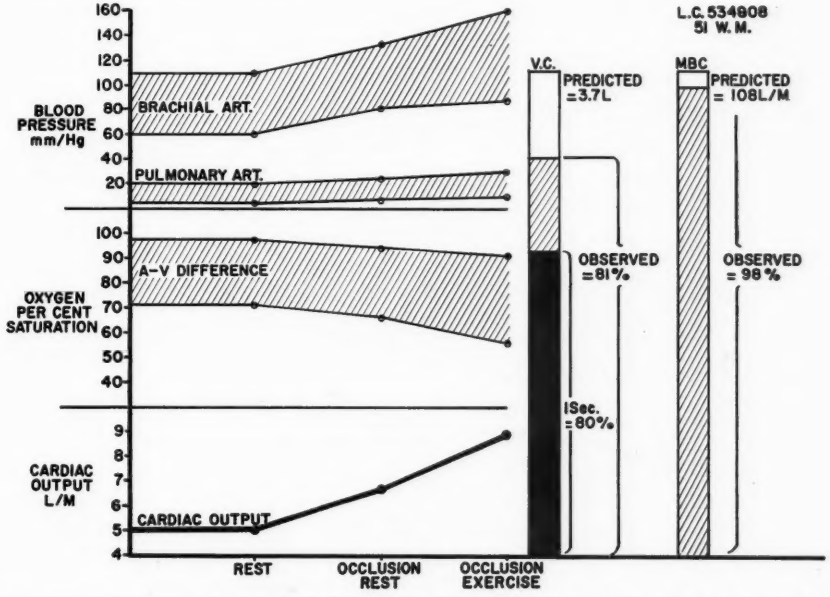

Fig. 1.—Left pulmonary artery occlusion. Normal response to temporary, unilateral occlusion of the pulmonary artery.

The difficulties encountered in using the balloon catheter were related to the larger size and the more complex construction of the catheter. There was an increased incidence of venous thrombosis in the arm and early studies were followed by pyrogenic reactions. Rupture of the balloon during inflation in one patient was followed by a chill and fever, but the patient had no symptoms at the time the balloon burst. In another patient, the partially inflated balloon slipped into the main pulmonary artery. This was recognized quickly and the balloon was deflated. While the balloon was in the main pulmonary artery the patient's condition remained unchanged.

The most frequent response to unilateral occlusion of the pulmonary artery is shown in Fig. 1. The patient was a 51-year-old white man in excellent general condition with a small, central carcinoma of the left lung. There

were metastases to the supraclavicular nodes. Studies showed that pulmonary function was not significantly reduced. With occlusion of the left pulmonary artery, there was a slight rise in the pulmonary artery and brachial artery pressures and a proportionate increase in the cardiac output and arteriovenous oxygen difference. The brachial artery oxygen saturation remained normal. While the left pulmonary artery was occluded, the patient was exercised. The pulmonary artery pressure rose to 36/12 mm. Hg and the brachial artery pressure to 152/76 mm. Hg. There was an additional increase in the arteriovenous oxygen difference and the cardiac output rose from a resting value of 5.1 L. per minute to 8.9 L. per minute. The brachial artery oxygen saturation remained normal.

An abnormal response to unilateral pulmonary artery occlusion was encountered in a 69-year-old man with carcinoma of the left lung and systemic hypertension. The data are charted in Fig. 2. There was a moderate reduction in pulmonary function, although the timed vital capacity was within normal limits. The pulmonary artery pressure was 20/6 mm. Hg at rest.

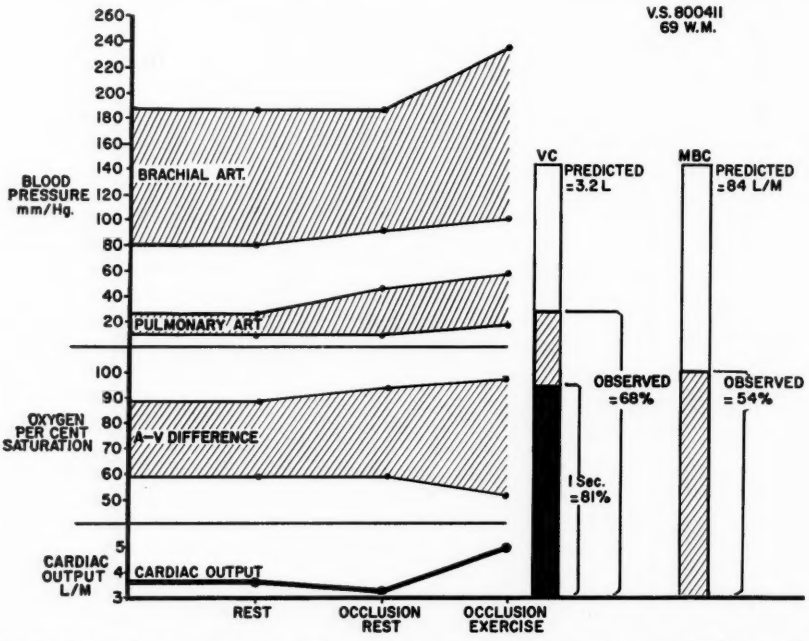

Fig. 2.—Left pulmonary artery occlusion. Abnormal response to temporary, unilateral occlusion of the pulmonary artery in a patient with impaired cardiovascular function.

It rose to 26/14 mm. Hg following occlusion of the left pulmonary artery. With exercise and occlusion of the pulmonary artery, the pulmonary artery pressure rose to 48/14 mm. Hg. This rise in pressure was not accompanied by a proportionate increase in the cardiac output but there was a marked increase in the arteriovenous oxygen difference. With exercise, the brachial artery oxygen saturation rose from 89 per cent to 96 per cent.

The rise in pulmonary artery pressure with pulmonary artery occlusion and exercise, the increase in the arteriovenous oxygen difference, and the slight rise in the cardiac output were believed to represent an inability to compensate for a reduction in the pulmonary vascular bed and an inability to increase the cardiac output with effort.

A left upper lobectomy was performed. The patient did well for a few days, but then became increasingly cyanotic and dyspneic. He died on the eleventh postoperative day. Death was believed to be due to progressive cardiorespiratory insufficiency. The post-mortem examination showed pulmonary emphysema and far-advanced generalized arteriosclerosis and arteriosclerotic heart disease with cardiomegaly.

The cardiovascular response of a second patient to occlusion of the right pulmonary artery was similar to that just described. This 65-year-old white man, with a history of asthma, had a carcinoma of the right lung. The patient's maximum breathing capacity was 68 per cent of the predicted normal value and his vital capacity was 92 per cent of the predicted normal value. A right upper lobectomy was performed. The patient developed pulmonary edema in the immediate postoperative period. He improved and his condition was satisfactory for several days. A bronchial leak required the reinsertion of a thoracotomy tube. The patient became increasingly cyanotic and dyspneic. He died seventeen days following operation. Permission for a post-mortem examination was not obtained.

These 2 patients had pulmonary function studies which were sufficiently good to have permitted a lobectomy to be done. The death of each patient was due, in part, to the inability of his cardiovascular system to compensate for the changes produced by operation.

The findings in a 49-year-old white man with carcinoma of the right lung are presented in Fig. 3. Although the vital capacity was 90 per cent of normal, the one second timed vital capacity and the maximum breathing capacity were reduced to 50 per cent of the predicted normal values. With occlusion of the right pulmonary artery and exercise, the cardiac output doubled without a marked increase in the pulmonary artery pressure. A right pneumonectomy was done and the patient recovered uneventfully despite the decrease in pulmonary function. The ability of the patient's cardiovascular system to compensate for a reduction in the pulmonary vascular bed may have contributed to the successful outcome.

Thirteen of the 18 patients studied were operated upon. In 7 patients, no resection was possible. Lobectomy was carried out in 4 patients and a pneumonectomy in 2 patients. No patient who had a normal response to unilateral pulmonary artery occlusion had complications during or after operation which could be attributed to cardiovascular insufficiency. One patient, a 19-year-old boy, had bilateral obstructive emphysema from bronchial compression by lymph nodes. During exercise, with occlusion of the right pulmonary artery, the pulmonary artery pressure rose to 72/20 mm. Hg. The patient did poorly during an operation in which lymph nodes compressing the bronchus intermedius were removed but he recovered after a stormy postoperative course.

None of the 18 patients studied had significant pulmonary hypertension at rest. Evidence of cardiovascular insufficiency and pulmonary hypertension was most striking when unilateral pulmonary artery occlusion was combined with exercise. A marked rise in pulmonary artery pressure, a greater increase in the arteriovenous oxygen difference, and a failure to increase the cardiac output indicated that the patient might not tolerate a pulmonary resection. The findings suggestive of cardiovascular insufficiency did not uniformly parallel reduction in ventilatory function.

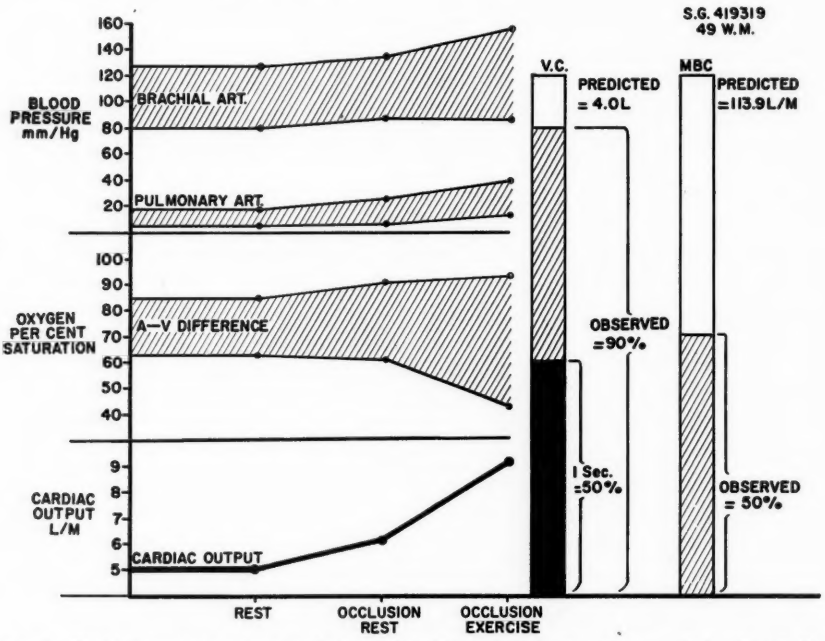

Fig. 3.—Right pulmonary artery occlusion. Normal response to temporary, unilateral occlusion of the pulmonary artery in a patient with decreased pulmonary function.

SUMMARY

1. Temporary occlusion of the right or left pulmonary artery with a balloon catheter was carried out successfully in 18 patients.

2. Unilateral occlusion of the pulmonary artery combined with exercise is a valuable method for studying the cardiovascular response to reduction in the pulmonary vascular bed.

3. In patients with impaired cardiovascular function, there is a marked rise in the pulmonary artery pressure, an abnormal increase in the arteriovenous oxygen difference, and a failure of the cardiac output to increase significantly when pulmonary artery occlusion is combined with exercise.

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DISCUSSION

DR. W. E. ADAMS, Chicago, Ill.—I should like to congratulate Dr. Sloan and his associates on what I consider a very fine study of an important problem. I think it has become apparent to us all that we are meeting this problem more and more as time goes on, due to lengthening of life expectancy.

Two years ago at the San Francisco meeting we made a report of some studies in dogs, on problems along this line, and subsequently have studied the problem in approximately 20 patients, either before, during, or following surgery. In 6 of these patients, a significant degree of pulmonary hypertension was either present before or increased sufficiently by pneumonectomy, and was the cause of death of 4 patients. An associated finding in some cases was the marked decrease in saturation of oxygen, which could be overcome easily by the administration of a small amount of oxygen by nasal catheter.

(slide) This is an example: This death occurred more than three weeks following operation. The patient had had a carcinoma of the lung which required pneumonectomy. He had had a hypertension of 39 cm. of water before surgery, which became elevated to 50 cm. after obstruction of the pulmonary artery. The blood oxygen saturation, even as long as thirteen days after operation, was below 80 per cent, whereas with only 1 L. of oxygen, this was elevated to almost 95 per cent.

(slide) With the recording oximeter which was developed by Dr. John F. Perkins, Jr., of our Physiology Department, one can study oxygen saturation quite easily on these patients, before, during, or after operation.

(slide) In one of these patients, the percentage of saturation of oxygen in the blood was below 70. With 1 L. of flow per minute, this was elevated to 96 per cent, which was almost as high as that obtained with 5 L. of oxygen per minute. How often one might see this associated low blood arterial oxygen saturation which becomes elevated with administration of very little oxygen, I do not know, but we have seen it in 4 or 5 patients and it might very well be that a study of this kind before operation, similar to the studies by catheterization as presented by Dr. Sloan, would help one materially in managing the treatment.

(slide) Here is the x-ray of this patient. He had a very small peripheral carcinoma; he was given pneumothorax to see if reduction in his total lung capacity could be tolerated. He actually went into cardiac failure. At operation, we removed much less than the entire lung and he slowly recovered. He is living without evidence of recurrence and doing fairly well, somewhat over a year following operation. This indicates to me that, if we have a choice as to the amount of lung to be resected in lesions either carcinomatous or otherwise, studies of this type may enable us to do a much better job for our patient.

CORONARY PERFUSION FOR LONGER PERIODS OF CARDIAC OCCLUSION UNDER HYPOTHERMIA*

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INTRODUCTION

CARDIAC occlusion under general hypothermia is a satisfactory method for performing operations of relatively short duration on the open heart. Despite the fact that Lewis used hypothermia to close successfully the first cardiac septal defect under direct vision in 1952, hypothermia has been utilized principally for juxtacardiac surgery.[1-3] Limited experience is reported with extension of low body temperature to intracardiac procedures more complicated than correction of atrial septal defects.[4, 5] Factors responsible for this limitation are related primarily to failure of the heart after prolonged periods of occlusion. Hypothermia seems to give less protection to the heart than to other important body systems probably because the heart extracts more oxygen from the blood than any other organ.[6] The period of cardiac occlusion from which recovery will regularly occur should be increased by adding coronary perfusion to supply the heart with oxygen.

Hypothermia not only protects the heart inadequately during periods of prolonged occlusion, but it also stimulates a relatively high incidence of ventricular fibrillation. In one-third of our clinical cases, ventricular fibrillation occurred at some time during the procedure; in only one was defibrillation unsuccessful. Swan[7] reported 100 per cent ventricular fibrillation in hypothermic dogs subjected to right ventriculotomy if neither Prostigmin nor acetylcholine was used to perfuse the heart prior to cardiotomy. Although defibrillation of the cold heart is not difficult, it is not enough to obtain survival if the incidence of ventricular fibrillation has been significant.

The design of these experiments with coronary perfusion was twofold: to prolong the period during which intracardiac surgery could be performed at safe levels of hypothermia, and to avert ventricular fibrillation by oxygenating the myocardium.

METHODS OF CORONARY PERFUSION IN THE DOG

The term indirect coronary perfusion is used to distinguish this technique from direct cannulation of the coronary arteries. All experiments were performed on adult dogs weighing from 25 to 80 pounds, anesthetized with pentobarbital sodium, and cooled to 25° C. Further details of cooling have been given elsewhere.[8]

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Read at the Thirty-fifth Annual Meeting of the American Association for Thoracic Surgery, Atlantic City, N. J., April 24 to 26, 1955.

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**U.S. Public Health Service, Research Fellow of the National Heart Institute.

Fig. 1 illustrates the anatomic considerations. Right thoracotomy is carried out through the fourth intercostal space. The azygos vein is divided between ligatures permitting mobilization of the superior vena cava. Elevation of the superior vena cava provides entrance into the posterior pericardium. A tourniquet for use during perfusion is loosely placed around the brachiocephalic artery at its junction with the aortic arch. The arch of the aorta is then cleared only enough to permit complete obstruction with a non-crushing clamp at a point between the brachiocephalic and left subclavian arteries. While the aortic clamp is momentarily closed, a No. 10 or 12 F. Bardic oxygen catheter is threaded into the ascending aorta via the right

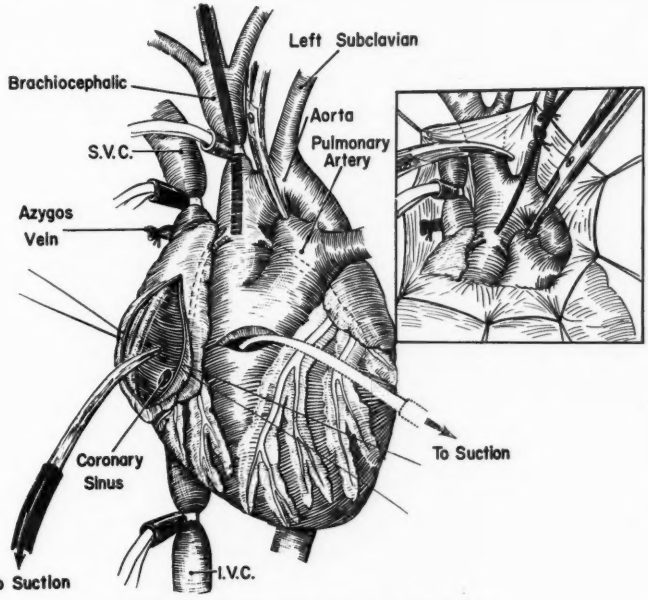

Fig. 1.—Technique of coronary perfusion.

carotid artery which is exposed through a small neck incision. With the anterior pericardium open, the catheter tip is palpated in the proximal aorta above the aortic valve. The catheter is then connected to the perfusion system, but perfusion does not begin until the venae cavae are occluded and outflow channels, distal to the catheter tip, are obstructed.

An alternate method is shown in the insert (Fig. 1). In the alternate method, cannulation is done within the chest utilizing the left subclavian artery. In this instance, the aorta is clamped distal to the left subclavian artery, and the brachiocephalic artery is occluded at its origin from the aortic arch.

The only circulation during the period of occlusion was that of the coronary perfusate which was pumped into the isolated proximal aorta by means of a finger pump.* As the perfusate entered the right heart via the

*Sigmamotor, Middleport, N. Y.

coronary sinus, the anterior coronary veins, and the Thebesian veins, it was aspirated through either a cardiotomy or an incision in the pulmonary artery.

The composition of the perfusate was altered from series to series and will be discussed separately. The flow rate was varied from 50 to 85 c.c. per minute. Pressures were measured in some experiments, and the range was from 25 to 85 mm. Hg. Pressures were related more to the strength of the heartbeat than to the flow rate at these slow rates of flow.

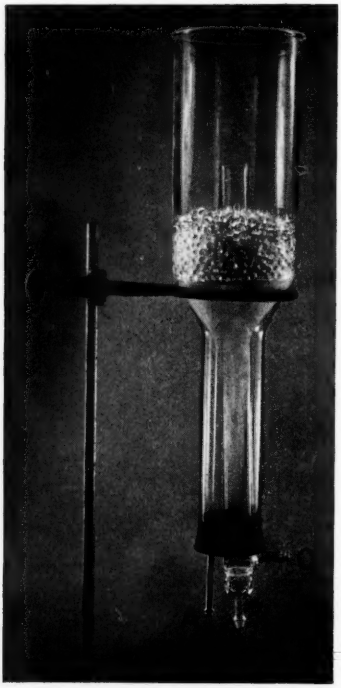

Fig. 2.—*A*, Outlet for blood from oxygenator. *B*, Oxygen inlet. *C*, Inlet for blood entering oxygenator.

INITIAL STUDY

At first, we thought it was necessary to obtain arterial levels of oxygen saturation in the blood to be used as perfusate. For this reason a modification of the Clark-Gollan gas dispersion apparatus was constructed.[9] This simple, bubble-type oxygenator, consisting of two concentrically placed glass cylinders, is seen in Fig. 2. Oxyygen introduced through a sintered glass disc in the bottom of the inner cylinder bubbled blood into the outer tube or reservoir ready for coronary perfusion. Glass beads coated with Antifoam A* were suspended in the outer tube by means of a stainless steel sieve. Blood was recirculated through the oxygenator after it had been aspirated from the heart so that the entire perfusion could easily be done with 500 c.c. of blood

*Dow-Corning Corp., Midland, Mich.

In the first two experiments, citrated blood was used but ventricular fibrillation occurred almost as soon as the perfusion was started. Cookson and co-workers[10] have called attention to this phenomenon. All further perfusions were performed with heparinized blood (20 mg. of heparin per 500 c.c. of blood).

Table I summarizes the results of the initial study. Immediate survival indicates that the animal regained normal temperature and was alive a minimum of 6 hours postoperatively. Late survival denotes that the dog was living at least one week following the procedure. Dogs were sacrificed after the one-week period in order to obtain blood for use in future studies.

TABLE I. CORONARY PERFUSION WITH OXYGENATOR BLOOD
INITIAL STUDY

CARDIAC APPROACH	NUMBER	IMMEDIATE SURVIVAL	LATE SURVIVAL	VENTRICULAR FIBRILLATION	TIME (MIN.)
Pulmonary arteriotomy	3	3	3	1	30
Right atriotomy	10	10	3	2	3 for 30
Right ventriculotomy	3	3	1	2	7 for 20
Total	16	16	7	5	20

The circulation was occluded in 6 dogs for 30 minutes and in 10 dogs for 20 minutes. Two of the former group had neurological impairment but none of the latter group did. In fact, neurological deficit was never observed in any dog with circulatory occlusion for 20 minutes at 25° C.

Our attention was not specifically attracted to bleeding difficulties although four deaths were attributed to hemorrhage complicated in one instance by empyema and atrial necrosis with perforation.

CLINICAL TRIAL

The perfect record of immediate survival and the relatively low incidence of ventricular fibrillation persuaded us to use coronary perfusion with the oxygenator clinically for the closure of two atrial septal defects under hypothermia.

The first case, that of a female child, proceeded successfully during the period of coronary perfusion but a postocclusion ventricular fibrillation developed as soon as cardiac massage was instituted for coronary air embolism. Incomplete expression of air from the left heart before closure of the defect may well have been responsible for the coronary air embolism. Defibrillation was easily done, and the patient seemed destined for an uneventful course. An unrelenting, hemorrhagic diathesis of mysterious origin, however, produced death eight hours postoperatively. Theoretically, and probably actually as well, no perfusate had escaped into the circulation.

The second case, that of a woman with a septum primum defect, was notable in that a disturbing flow of blood obscured the operative field which made identification of the structures difficult. Complete closure of the defect was obtained in 7 minutes, but again postocclusion ventricular fibrillation developed. Defibrillation was immediately effected, and the heart responded well during the remainder of the operative period. An excessive amount of chest drainage necessitated thoracic exploration six hours postoperatively.

Bleeding appeared to come from many small sources rather than from any single site. Following the second operation, chest drainage diminished slowly and the patient recovered fully.

The flow rate for each case was close to 100 c.c. per minute. Blood was not recirculated through the oxygenator. The hearts were pink and apparently well oxygenated during the perfusions. Cannulation was done through the left subclavian artery. Although both hearts fibrillated, the ease of defibrillation was remarkable. Before further clinical application could be advocated, however, a more critical laboratory evaluation was necessary.

SECOND STUDY

In the second series of animal experiments, we were seeking in particular any characteristics of the technique which might explain the bleeding tendency which had appeared clinically. Both the oxygenator and the technique were under scrutiny. To make the experiments more similar to the clinical situation coronary drainage was aspirated and discarded rather than recirculated through the oxygenator. The animals were carefully followed postoperatively and given transfusions when it was indicated. Table II outlines the results obtained in 7 consecutive dogs with 20 minutes of circulatory occlusion and coronary perfusion.

TABLE II. CORONARY PERFUSION WITH OXYGENATOR BLOOD
SECOND STUDY

CARDIAC APPROACH	NUMBER	IMMEDIATE SURVIVAL	LATE SURVIVAL	VENTRICULAR FIBRILLATION	TIME (MIN.)	WHOLE BLOOD TRANSFUSION
Right atriotomy	7	7	7	0	20	4

Transfusions were necessary in 4 of the 7 animals, and 1 dog received 800 c.c. of blood to replace loss from the chest cavity. Protamine, which was given in each case (50 to 150 mg.), seemed to have little effect on the persistence of chest drainage. Bleeding eventually subsided in all experimental cases, and the late survival rate of 100 per cent was undoubtedly the result of intensified postoperative care.

Clotting factors were checked as well as platelet count, plasma hemoglobin, hydrogen ion concentration (pH), and oxygen content on blood entering and leaving the oxygenator. Samples of coronary drainage were also analyzed for oxygen saturation to ascertain roughly the myocardial oxygen consumption. In general, there was a small increase in the clotting time after perfusion, but no increase in prothrombin time was detected in any of the 3 dogs whose prothrombin time was determined. The entire laboratory analysis of this series is given in Table III. Platelet counts were insignificantly diminished by the action of the oxygenator. Plasma hemoglobin was always higher in blood coming from the oxygenator but never greater than 147 mg. per cent. The pH shift was toward the alkaline side with 7.63 the most alkaline pH of blood leaving the machine. Oxygen contents were uniformly elevated to approximately 20 volumes per cent by the oxygenator depending on the hemoglobin concentration. Oxygen saturation of the coronary drainage averaged 5.4 volumes per cent less than the perfusate, but the range was wide depending on the cardiac activity when the sample was taken.

TABLE III. CORONARY PERFUSION WITH OXYGENATOR BLOOD
LABORATORY RESULTS OF SECOND STUDY

	DOG NO.													
	1		2		3		4		5		6		7	
	A*	B*	A	B	A	B	A	B	A	B	A	B	A	B
Oxygen content vol. %	8.1	19.7	14.2	19.9	10.7	22.5	14.3	22.3	13.2	21.0	15.4	20.6	13.45	19.88
Hgb. Gm. %	–	–	13.6	13.9	15.0	15.0	14.7	14.6	13.1	12.8	13.1	13.1	12.0	12.1
Plasma hgb. mg. %	18	36	9	20	10	–	67	147	38	43	18	58	5	23
Platelets in 1,000's	146	132	276	230	224	232	224	164	154	152	138	112	89	140
pH	7.41	7.52	7.33	7.53	7.33	7.49	7.35	7.63	7.34	7.53	7.28	7.54	7.36	7.59
Oxygen content of coronary drainage vol. %	16.9		16.8		20.1		15.2		10.1		10.1		19.18	
Clotting time before perfusion	–		Lee-White 14 min.		Lee-White 14 min.		capillary 5 min.		capillary 5 min.		capillary 4.5 min.		capillary 3.5 min.	
Clotting time after perfusion	–		Lee-White 35 min.		Lee-White 45 min.		capillary 14.5 min.		capillary 12 min.		capillary 5 min.		capillary 4.5 min.	
Prothrombin time after perfusion	–		No increase		No increase		No increase		–		–		–	
Flow rate c.c. per min.	80		80		80		50		50		50		85	

*A, Blood to oxygenator.
B, Blood from oxygenator.

Very little could be found to explain the postperfusion bleeding encountered clinically and in some of the dogs. Elevation of clotting time seemed to depend on how carefully one aspirated the perfusate thus preventing escape into the pulmonary circuit. Neither clinical case manifested any increase in clotting time. The exact cause of the bleeding tendency remained obscure although the glass composition of the oxygenator may have played a part.[11] Apparently cardiac perfusion itself was enough to transmit the hemorrhagic diathesis to the animal since very little perfusate was permitted to enter the circulation.

CORONARY PERFUSION WITH VENOUS BLOOD

Because of the low oxygen utilization by the empty, hypothermic heart, it was felt that blood with venous levels of oxygen saturation would maintain a reasonable degree of myocardial oxygenation during perfusion. Table IV describes the results of 10 consecutive coronary perfusions with venous blood.

TABLE IV. CORONARY PERFUSION WITH VENOUS BLOOD

CARDIAC APPROACH	NUMBER	IMMEDIATE SURVIVAL	LATE SURVIVAL	VENTRICULAR FIBRILLATION	TIME (MIN.)	WHOLE BLOOD TRANSFUSION
Right atriotomy	5	5	5	0	20	0
Right ventriculotomy	5	5	5	2	20	0
Total	10	10	10	2		0

No blood transfusions were needed. All animals survived indefinitely after cardiac occlusion for 20 minutes at 25° C. Ventricular fibrillation occurred in only 2 animals. Venous blood was drawn from donor animals by means of a femoral vein catheter. Flow rates were always 50 c.c. per minute so that two 500 c.c. bottles of heparinized blood were sufficient for the 20 minutes of perfusion. Oxygen contents were determined on each bottle of blood before perfusion and on the coronary drainage; the values are listed in Table V.

TABLE V. CORONARY PERFUSION WITH VENOUS BLOOD
OXYGEN CONTENT VOLUME PER CENT

	DOG NO.									
	1	2	3	4	5	6	7	8	9	10
Bottle 1										
Before perfusion	8.56	11.08	10.20	11.61	11.40	5.81	9.64	10.42	9.38	6.93
Coronary drainage	2.33	7.42	3.90	6.25	11.19	2.54	3.68	1.94	5.72	2.01
Bottle 2										
Before perfusion	9.21	10.99	4.00	10.87	12.19	7.45	11.34	16.31	15.78	12.61
Coronary drainage	4.59	7.95	0.88	4.82	7.71	5.21	7.98	9.14	11.25	8.17

The lowest oxygen content of any perfusate was 4 volumes per cent with the heart consuming all but 0.88 volume per cent of the available oxygen. Coronary drainage averaged 4.4 volumes per cent less in oxygen content than the perfusate. In 1 dog, ventricular fibrillation occurred as the catheter was threaded into the aorta; defibrillation was quickly done after which the animal withstood 20 minutes of cardiac occlusion and right ventriculotomy without relapse into fibrillation.

DISCUSSION

The fact that the heart extracts more oxygen from the blood than any other organ in the body is the basis for attempting to prolong, by means of coronary

perfusion, the period of cardiac occlusion from which animals consistently recover. By protecting the heart with oxygen, brain tolerance to circulatory interruption becomes the factor which determines the safe period of cardiac occlusion under hypothermia. Full advantage of the time allowed by resistance of the nervous system to hypoxia at low temperatures has not previously been taken because of failure of the heart to survive. Perfusing the heart with blood containing even venous levels of oxygen permits 20 minutes of occlusion in the dog at 25° C. without evidence of neurological damage.

The best results with hypothermia in experimental surgery are obtained at temperatures well above 20° C. Bigelow and associates[12] had only 6 final survivors in 39 dogs with 15 minutes of cardiac occlusion at 20° C. Our experiments indicate that prolonged cardiac occlusion is possible at a safe level of hypothermia if the myocardium is oxygenated. Bigelow has maintained that complicated intracardiac surgery necessitates 20 minutes of circulatory occlusion at 20° C., a temperature too dangerous for clinical use.[13] We feel that the repair of such conditions as interventricular septal defects can be done within the time permitted by safe levels of hypothermia particularly if the heart is protected by coronary perfusion.

Cookson and Costas-Durieux[14] have stated that cardiac perfusion pressures should be in the range of 70 mm. Hg to prevent coronary air embolism and that a nonpulsatile flow is necessary to avoid aortic regurgitation. Despite these measures, 2 of his 11 dogs suffered coronary air embolism. Momentary, supravalvular occlusion of the aorta to provide a dry operative field during full body perfusions has not predisposed to coronary air embolism in the presence of ventricular septal defects.[15] The necessity for a nonpulsatile flow at a relatively high pressure probably does not exist when the heart is empty and the pressures generated by cardiac action decreased. The principal danger of coronary air embolism is incomplete evacuation of air from the heart before closure of the defect and the cardiotomy.

Ventricular fibrillation occurred in only 2 of 17 consecutive experiments. While coronary perfusion did not preclude ventricular fibrillation, the incidence was well within an acceptable range. Dogs at normal temperatures frequently respond to right ventriculotomy by developing fibrillation; hence, abolition of ventricular fibrillation in any series of cardiotomies is rather unlikely.

SUMMARY AND CONCLUSIONS

1. Coronary perfusion can prolong the period of cardiac occlusion under hypothermia.

2. At 25° C. the central nervous system can tolerate 20 minutes of circulatory interruption without evident neurological damage.

3. A bubble-type oxygenator made of glass produces bleeding even when all or nearly all perfusate is aspirated from the heart.

4. Coronary perfusion with venous blood at a flow rate of 50 c.c. per minute is satisfactory for maintaining an acceptable degree of myocardial oxygenation.

5. Protection from ventricular fibrillation is demonstrated by the consecutive, long-term survival of 12 dogs undergoing 20 minutes of cardiac occlusion at 25° C. and right atriotomy without ventricular fibrillation.

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DISCUSSION

DR. OSLER ABBOTT, Emory University, Ga.—I believe we should place some emphasis on the following problem which was presented to us rather dramatically in a patient. This was a patient with a thoracic aortic aneurysm wherein preoperative studies could not define whether there was need for resection of a segment of the aorta with temporary occlusion of aortic blood flow or just an amputation of the sac without aortic occlusion. At operation aortic occlusion proved necessary. Hypothermia was produced by externally circulating blood utilizing a Sigmamotor pump, the tubing of which was imbedded in coils of ice. The tubes had been primed with heparin and the patient had a total dosage of 25 mg. of this drug. The aorta was occluded just distal to the left subclavian artery, and citrated blood replacement was given. The hypothermia and aortic occlusion produced a major degree of hypotension within the liver bed. A clinical syndrome, of irreversible character, was produced in this patient, simulating exactly the findings that Brindley has reported in total hepatectomy of dogs. Laboratory tests of this patient's blood showed complete prolongation of prothrombin time, citrate poisoning with severe calcium depletion, and irreversible heparinization. We agree, therefore, with the article presented in a recent issue of the *Journal of the American Medical Association* on citrate poisoning as a major hazard of hypothermia with associated decrease in circulation to the liver. Any transfusions used in such physiologic preparations should be prepared by means of a resin membrane to remove the calcium from the blood so as not to subject the patient to quantities of citrate or heparin which the liver cannot detoxify.

BLOOD VOLUME STUDIES IN THORACIC SURGICAL PATIENTS USING RADIOACTIVE IODINATED HUMAN SERUM ALBUMIN (RIHSA)

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THE importance of a normal preoperative blood volume with adequate replacement of blood lost during and after major operative procedures is recognized by all surgeons. The surgeon often relies on his clinical acumen and a routine blood count and hematocrit as to the blood requirements of the patient before, during, and after major surgery. The use of these methods of appraisal has resulted in serious untoward consequences for some patients due to the administration of too little or too much blood.

There are a number of substances, isotopic and otherwise, as well as techniques by which the blood volume, plasma volume, and red-cell volume may be determined. The early studies of blood loss during surgery involved the use of colorimetric (acid hematin)[1] or gravimetric (weighed sponge)[2, 3] methods. These techniques are useful and their practical value is recognized, but numerous studies have shown that they do not possess a high degree of accuracy. When compared with simultaneous estimations of the blood volume utilizing more precise methods, it has been shown that there is a postoperative reduction in the blood volume of from 30 to 50 per cent more than one would anticipate on the basis of the blood loss estimated gravimetrically or colorimetrically.[4-6] In addition to the blood loss during the surgical procedure, it has been established that there is continued loss of red-blood cells in the postoperative period; at times the postoperative blood loss may equal or even exceed that lost during the operation.[4-7]

Previous investigators of this problem have used a dye dilution method employing Evans blue dye (T-1824), P^{32} labeled erythrocytes, or radioactive iodinated human serum albumin (RIHSA) in their studies. Although we have used RIHSA most often, we have also determined the blood volume using P^{32} and Cr^{51} tagged erythrocytes. In a number of patients, we have employed Cr^{51} and RIHSA simultaneously, the former for the red-cell volume and the latter for the plasma volume, the sum of these values being the blood volume. As one would expect, the values for each of the above volumes depend upon whether one compartment (plasma or cells) is determined directly and the other two indirectly from it and the hematocrit, or whether both compartments are determined independently.

The opinions or assertions contained herein are those of the authors and are not to be construed as official or reflecting the views of the Navy Department or of the naval service at large.

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TABLE I. SEGMENTAL RESECTION

PATIENT	DIAGNOSIS	SITE	IMMEDIATE PREOPERATIVE VALUES				GIVEN AT OPERATION	IMMEDIATE POSTOPDRATIVE VALUES				ONE WEEK POSTOPERATIVE VALUES			
			BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)	BLOOD (C.C.)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)
D. F.	Tbc.	LLL	5368	2947	2421	45.1	1500	3932	2556	1376	35.0	4425	3022	1403	31.7
A. D.	Tbc.	RUL	5652	2730	2922	51.7	1000	4838	2298	2540	52.5	4508	2655	1853	41.1
L. D.	Tbc.	LUL	5377	2984	2393	44.5	1000	5047	2978	2069	41.0	5254	3184	2070	39.4
R. C.	Tbc.	RUL	6672	3503	3169	47.5	1000	4683	2557	2126	45.4	5721	3381	2340	40.9
N. B.	Tbc.	RUL	4599	2437	2162	47.0	1000	4066	2285	1781	43.8	4423	2729	1694	38.3
H. E.	Tbc.	RUL	3257	1668	1589	48.8	1500	3521	2049	1472	41.8	3980	2304	1676	42.1
C. R.	Tbc.	LUL	5221	2877	2344	44.9	1500	4048	2259	1789	44.3	4292	2983	1309	30.5
W. L.	Tbc.	LLL	4908	2748	2160	44.0	1500	3934	2274	1660	42.2	4373	2694	1679	38.4
C. K.	Tbc.	RUL	5230	2563	2667	51.0	1000	4498	2339	2159	48.0	4814	2772	2042	42.4
E. R.	Tbc.	RUL	5871	2965	2906	49.5	1500	4834	2550	2288	47.3	5465	3219	2246	41.1
J. C.	Tbc.	RUL	5297	3099	2198	41.5	2000	4956	2954	2002	40.4	4434	2589	1845	41.6
R. S.	Tbc.	RUL	7408	3904	3504	47.3	1000	6406	3370	3036	47.4	6918	3736	3182	46.0
P. B.	Tbc.	RUL	5180	3056	2124	41.0	2000	4307	2662	1645	38.2	4594	3096	1498	32.6
D. M.	Tuberculoma	RUL	6821	3438	3383	49.6	1000	6422	3153	3269	50.9	5307	3067	2240	42.2
D. S.	Tbc.	LUL	5331	3044	2287	42.9	2500	4546	2609	1937	42.6	5114	3247	1867	36.5
J. M.	Tbc.	LUL	4871	2635	2236	45.9	1000	4365	2457	1908	43.7	3506	1963	1543	44.0
W. F.	Fibrocaseous granuloma	RUL	5737	3127	2610	45.5	1000	5127	2666	2461	48.0	5667	3338	2329	41.1
J. H.	Tbc.	LUL	5545	2983	2562	46.2	2000	4251	2550	1701	40.4	4883	4130	1743	35.7
M. B.	Bronchiectasis	LUL	3588	2121	1467	40.9	1500	3185	1844	1341	42.1	3465	2020	1445	41.7
W. J.	Tbc.	RUL	5101	2530	2571	50.4	1500	4734	2239	2495	52.7	4976	2727	2249	45.2
V. S.	Tbc.	RUL	6163	3310	2853	46.3	1500	5683	3200	2483	43.7	6348	4190	2158	34.0
P. Y.	Tbc.	RUL	5917	2994	2923	49.4	1500	5562	2653	2909	52.3	5886	3178	2708	46.0
W. T.	Tbc.	RUL	5910	3162	2748	46.5	2000	4756	2673	2083	43.8	5569	3464	2105	37.8
J. K.	Tbc.	RUL	5641	2804	2837	50.3	1000	4948	2583	2365	47.8	6137	3688	2449	39.9
C. C.	Tbc.	RUL	5643	2889	2754	48.8	500	5224	2775	2449	46.8	5913	3441	2472	41.8
R. F.	Tbc.	RUL	5944	3198	2746	46.2	1000	4852	2746	2106	43.4	6040	3630	2410	39.9
H. G.	Fibrocaseous granuloma	RUL	5526	2669	2857	51.7	1100	6312	3206	3106	49.2	6378	3246	3132	49.1
K. H.	Tbc.	RUL	5869	3375	2494	42.5	1000	5806	3350	2456	42.3	5879	3886	1993	33.9
J. H.	Fibrocaseous granuloma	LUL	4958	2628	2330	47.0	1000	5377	2855	2522	46.9	5785	3083	2702	46.7
C. J.	Tbc.	RUL	4862	2801	2061	42.4	500	4884	2774	2110	43.2	5576	3212	2364	42.4
J. K.	Tbc.	RUL	6189	3435	2754	44.5	1000	6254	3308	2946	47.1	7131	4143	2988	41.9
J. C.	Tbc.	LUL	6082	3400	2682	44.1	1500	5396	3184	2212	41.0	6532	4050	2482	38.0

D. R.	Tbc.	LUL	4462	2253	2209	49.5	1000	4507	2740	1767	39.2	4446	2717	1729	38.9
J. M.	Tbc.	LUL	5802	3191	2611	45.0	1000	4933	2787	2146	43.5	5887	3615	2272	38.6
K. J.	Tbc.	LUL	5997	3160	2837	47.3	1000	5856	3074	2782	47.5	6071	3521	2550	42.0
J. H.	Tbc.	RUL	5979	3169	2810	47.0	1000	5526	3084	2442	44.2	5178	3008	2170	41.9
J. L.	Tbc.	RUL	4038	2310	1728	42.8	1500	3513	1978	1535	43.7	3998	2547	1451	36.3
P. Y.	Tbc.	LLL	6145	3036	3109	50.6	1000	5404	2686	2718	50.3	5610	3209	2401	42.8
B. S.	Tbc.	RUL	3167	1919	1248	39.4	2000	3304	1986	1318	39.9	3689	2324	1365	37.0
R. E.	Tbc.	LUL	4447	2357	2090	47.0	1000	4436	2373	2063	46.5	4733	2726	2007	42.4
C. B.	Tbc.	RUL	5158	2703	2455	47.6	1000	4657	2561	2096	45.0	5251	3245	2006	38.2
C. W.	Tbc.	RUL	3801	2167	1634	43.0	1000	3666	2148	1518	41.4	4926	3493	1433	29.1
H. K.	Tbc.	LUL	3637	1949	1688	46.4	950	3677	2228	1449	39.4	3924	2515	1409	35.9
L. G.	Tbc.	RUL	5523	2795	2728	49.4	1000	5338	2664	2674	50.1	5621	3232	2389	42.5
Average			5316	2842	2474	46.4	1251	4808	2642	2166	44.7	5196	3119	2077	39.8

The purpose of this report is to describe the blood volume changes in a group of 65 patients who underwent excisional pulmonary surgery. Radioactive iodinated human serum albumin was used in all of these studies. The operations performed consisted of 44 segmental resections, 8 lobectomies, 8 wedge resections, and 5 local enucleations. Three blood volume determinations were done in each case. These studies were carried out one or two days preoperatively, immediately after operation, and 7 days postoperatively.

MATERIALS AND METHODS

The radioactive iodinated human serum albumin (RIHSA) was obtained from Abbott Laboratories, Chicago, Illinois. Using 0.85 per cent salt solution as the diluent, a 5 per cent solution of normal human serum albumin was made which contained 2 microcuries of RIHSA per cubic centimeter. From a calibrated syringe, between 10 and 20 c.c. of the above solution were injected into a vein. Approximately 20 microcuries of RIHSA were used for each determination. After an interval of 10 minutes, 10 c.c. of blood was withdrawn without stasis from an antecubital vein in the opposite arm. Potassium and ammonium oxalates were used as the anticoagulant. Prior to each subsequent blood volume determination, a specimen of blood was obtained to correct for residual activity from the preceding study.

Hematocrits were obtained in duplicate, using Wintrobe hematocrit tubes, and the average value was used in the computations. Three cubic centimeter aliquots of whole blood were pipetted into small glass vials and inserted into a well-type scintillation counter. The crystal used was 35 per cent efficient for I^{131} gamma rays and was not volume sensitive between 1 and 4 c.c. Two aliquots were obtained from each blood specimen and each aliquot was counted twice. For the control, a 1:500 dilution of the injection solution was used. Duplicate 3 c.c. aliquots were counted twice with each blood volume determination. The counting error for the whole blood specimen and control was 3 per cent or less.

Calculation of the blood volume, plasma volume, and red-cell volume was performed as follows:

$$\text{Blood volume} = \frac{\text{Net counts/minute/c.c. control} \times 500 \times \text{c.c. injected}}{\text{Net counts/minute/c.c. whole blood}}$$

$$\text{Plasma volume} = \text{Blood volume} \times \text{plasmacrit}$$

$$\text{Red-cell volume} = \text{Blood volume} \times \text{hematocrit}$$

The amount of blood lost during the operation was taken to be the difference between the preoperative and immediate postoperative blood volumes plus the amount of blood given at surgery. The seventh postoperative day blood volume minus the immediate postoperative value represents the blood lost or gained during the first postoperative week. The seventh postoperative day blood volume less the preoperative blood volume is the blood excess or deficit, relative to the preoperative value, at the end of the first postoperative week. Changes in the plasma and red-cell volumes were calculated similarly. In no instance was a blood volume determination performed while the patient was receiving blood. No patient received blood or plasma between the first

and third blood volume determinations except at surgery. All estimated blood losses during surgery were obtained by the dry weighed sponge technique plus suction bottle contents. It was assumed that each 500 c.c. of whole blood transfused contained 200 c.c. of red cells and 300 c.c. of plasma. Tables I through VIII list the patients, their diagnoses, the operations performed, and the observed blood volume changes.

RESULTS

TABLE II. SEGMENTAL RESECTION

PATIENT	ESTIMATED* LOSS AT OPERATION	GIVEN AT OPERATION	ACTUAL LOSS AT OPERATION			GAIN OR LOSS—FIRST POSTOPERATIVE WEEK			EXCESS OR DEFICIT—ONE WEEK POSTOPERATIVE VS. PREOPERATIVE		
	BLOOD (C.C.)	BLOOD (C.C.)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)
D. F.	850	1500	2936	1291	1645	+493	+466	+27	-943	+75	-1018
A. D.	900	1000	1814	1032	782	-330	+357	-687	-1144	-75	-1069
L. D.	800	1000	1330	606	724	+207	+206	+1	-123	+200	-323
R. C.	500	1000	2989	1546	1443	+1038	+824	+214	-951	-122	-829
N. B.	800	1000	1533	752	781	+357	+444	-87	-176	+292	-468
H. E.	1000	1500	1236	519	717	+459	+255	+204	+723	+636	+87
C. R.	1200	1500	2673	1518	1155	+244	+724	-480	-929	+106	-1035
W. L.	1200	1500	2474	1374	1100	+439	+420	+19	-535	-54	-481
C. K.	750	1000	1732	824	908	+316	+433	-117	-416	+209	-625
E. R.	1600	1500	2533	1315	1218	+627	+669	-42	-406	+254	-660
J. C.	1200	2000	2341	1345	996	-522	-365	-157	-863	-510	-353
R. S.	800	1000	2002	1134	868	+512	+366	+146	-490	-168	-322
P. B.	1400	2000	2873	1594	1279	+287	+434	-147	-586	+40	-626
D. M.	800	1000	1399	885	514	-1115	-86	-1029	-1514	-371	-1143
D. S.	2000	2500	3285	1935	1350	+568	+638	-70	-217	+203	-420
J. M.	850	1000	1506	778	728	-859	-494	-365	-1365	-672	-693
W. F.	?	1000	1610	1061	549	+540	+672	-132	-70	+211	-281
J. H.	?	2000	3294	1633	1661	+632	+590	+42	-662	+157	-819
M. B.	?	1500	1903	1177	726	+280	+176	+104	-123	-101	-22
W. J.	?	1500	1867	1191	676	+242	+488	-246	-125	+197	-322
V. S.	?	1500	1980	1010	970	+665	+990	-325	+185	+880	-695
P. Y.	?	1500	1855	1241	614	+324	+525	-201	-31	+184	-215
W. T.	?	2000	3154	1689	1465	+813	+791	+22	-341	+302	-643
J. K.	900	1000	1693	821	872	+1189	+1105	+84	+496	+884	-388
C. C.	520	500	919	414	505	+689	+666	+23	+270	+552	-282
R. F.	?	1000	2092	1052	1040	+1188	+884	+304	+96	+432	-336
H. G.	700	1100	314	123	191	+66	+40	+26	+852	+577	+275
K. H.	1000	1000	1063	625	438	+73	+536	-463	+10	+511	-501
J. H.	?	1000	581	373	208	+408	+228	+180	+827	+455	+372
C. J.	650	5000	478	327	151	+692	+438	+254	+714	+411	+303
J. K.	650	1000	935	727	208	+877	+835	+42	+942	+708	+234
J. C.	?	1500	2186	1116	1070	+1136	+866	+270	+450	+650	-200
D. R.	580	1000	955	113	882	-61	-23	-38	-16	+464	-480
J. M.	?	1000	1869	1004	865	+954	+828	+126	+85	+424	-339
K. J.	920	1000	1141	686	455	+215	+447	-232	+74	+361	-287
J. H.	900	1000	1453	685	768	-348	-76	-272	-801	-161	-640
J. L.	450	1500	2025	1232	793	+485	+569	-84	-40	+237	-277
P. Y.	?	1000	1741	950	791	+206	+523	-317	-535	+173	-708
B. S.	?	2000	1863	1133	730	+385	+338	+47	+522	+405	+117
R. E.	650	1000	1011	584	427	+297	+353	-56	+286	+369	-83
C. B.	700	1000	1501	742	759	+594	+684	-90	+93	+542	-449
C. W.	?	1000	1135	619	516	+1260	+1345	-85	+1125	+1326	-201
H. K.	750	950	910	291	619	+247	+287	-40	+287	+566	-279
L. G.	700	1000	1185	731	454	+283	+568	-285	+98	+437	-339
Average	891†	1251	1759	950	809	+388	+477	-89	-120	+277	-397

*According to weighed sponge technique.
†Based on 30 patients.

TABLE III. LOBECTOMY

PATIENT	DIAGNOSIS	SITE	IMMEDIATE PREOPERATIVE VALUES				GIVEN AT OPERATION	IMMEDIATE POSTOPERATIVE VALUES				ONE WEEK POSTOPERATIVE VALUES			
			BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)	BLOOD (C.C.)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)
E. H.	Tbc.	RUL	6079	3362	2717	44.7	1510	5187	2900	2287	44.1	6084	3882	2202	36.2
H. E.	Tbc.	LLL	5399	2915	2484	46.0	500	5154	2871	2283	44.3	4874	3183	1691	34.7
D. G.	Tbc.	LLL	5481	2949	2532	46.2	1000	5842	3009	2833	48.5	5405	3102	2303	42.6
H. W.	Fibrocaseous granuloma	RLL	4392	2257	2135	51.4	1500	3984	2016	1968	49.4	4351	2332	2019	46.4
J. C.	Tbc.	RUL	5800	2964	2836	48.9	1500	5827	3135	2692	46.2	5651	3351	2300	40.7
P. D.	Tbc.	RLL	3066	2140	926	30.2	1500	3226	2032	1194	37.0	3719	2503	1216	32.7
J. P.	Tbc.	RUL	5367	2823	2544	47.4	2500	4139	2268	1871	45.2	4870	3326	1544	31.7
J. S.	Bronchiectasis	RML RLL	5975	3322	2653	44.4	2000	5241	2904	2337	44.6	5734	3440	2294	40.0
Average			5195	2842	2353	44.9	1500	4825	2642	2183	44.9	5086	3140	1946	38.1

TABLE IV. LOCAL ENUCLEATION

PATIENT	DIAGNOSIS	SITE	IMMEDIATE PREOPERATIVE VALUES				GIVEN AT OPERATION	IMMEDIATE POSTOPERATIVE VALUES				ONE WEEK POSTOPERATIVE VALUES			
			BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)	BLOOD (C.C.)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)
L. S.	Fibrocaseous granuloma		5642	3064	2578	45.7	500	5570	2913	2657	47.7	6561	3819	2742	41.8
D. B.	Fibrocaseous granuloma		5142	2715	2427	47.2	500	4870	2635	2235	45.9	5089	2890	2199	43.2
D. T.	Tuberculoma	RLL	5494	3038	2456	44.7	1000	4244	2351	1893	44.6	5662	3516	2146	37.9
J. P.	Fibrocaseous granuloma	LUL	5373	3057	2316	43.1	500	4421	2661	1760	39.8	5182	3249	1933	37.3
J. H.	Granuloma, type undetermined	Lingula	6491	3486	3005	46.3	500	6296	3438	2858	45.4	5820	3376	2444	42.0
Average			5628	3072	2556	45.4	600	5080	2800	2280	44.7	5662	3370	2292	40.4

TABLE V. WEDGE RESECTION

PATIENT	DIAGNOSIS	SITE	IMMEDIATE PREOPERATIVE VALUES				GIVEN AT OPERATION	IMMEDIATE POSTOPERATIVE VALUES				ONE WEEK POSTOPERATIVE VALUES			
			BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)	BLOOD (C.C.)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)	BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	HEMATOCRIT (%)
R. A.	Tbc.	LUL LLL	6355	3279	3076	48.4	2000	5469	3123	2346	42.9	6910	4429	2481	35.9
E. F.	Tbc.	RUL	4709	2552	2157	45.8	1000	5244	2842	2402	45.8	4727	2685	2042	43.2
V. M.	Tbc.	LUL	5352	2879	2473	46.2	500	4990	2695	2295	46.0	5646	3348	2298	40.7
S. S.	Tbc.	LUL	6023	3162	2861	47.5	1000	6335	3446	2889	45.6	6317	3740	2577	40.8
A. M.	Tbc.	RUL	5715	3155	2560	44.8	1000	6058	3750	2308	38.1	6355	3978	2377	37.4
G. P.	Congenital cystic disease	LLL	4678	2503	2175	46.5	1000	4337	2459	1878	43.3	5023	3074	1949	38.8
J. V.	Tbc.	LUL	4378	2141	2237	51.1	500	4578	2391	2187	47.8	5007	2704	2303	46.0
J. H.	Tbc.	RUL	5394	2864	2530	46.9	500	5261	2883	2378	45.2	6231	3963	2268	36.4
Average			5326	2817	2509	47.1	937	5284	2949	2335	44.3	5777	3490	2287	39.9

TABLE VI. LOBECTOMY

PATIENT	ESTIMATED* LOSS AT OPERATION BLOOD (C.C.)	GIVEN AT OPERATION BLOOD (C.C.)	ACTUAL LOSS AT OPERATION BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	GAIN OR LOSS—FIRST POSTOPERATIVE WEEK BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	EXCESS OR DEFICIT—ONE WEEK POSTOPERATIVE VS. PREOPERATIVE BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)
H. E.	1200	1500	2392	1362	1030	+897	+982	−85	+5	+520	−515
D. G.	294	500	745	344	401	−280	+312	−592	−525	+268	−793
E. H.	800	1000	639	540	99	−437	+93	−530	−76	+153	−229
H. W.	1100	1500	1908	1141	767	+367	+316	+51	−41	+75	−116
J. C.	1300	1500	1473	729	744	−176	+216	−392	−149	+387	−536
P. D.	1450	1500	1340	1008	332	+493	+471	+22	+653	+363	+290
J. P.	2000	2500	3728	2055	1673	+731	+1058	−327	−497	+503	−1000
J. S.	1570	2000	2734	1618	1116	+493	+536	−43	−241	+118	−359
Average	1214	1500	1870	1100	770	+261	+498	−237	−109	+298	−407

*According to weighed sponge technique.

TABLE VII. LOCAL ENUCLEATION

PATIENT	ESTIMATED* LOSS AT OPERATION BLOOD (C.C.)	GIVEN AT OPERATION BLOOD (C.C.)	ACTUAL LOSS AT OPERATION BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	GAIN OR LOSS—FIRST POSTOPERATIVE WEEK BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	EXCESS OR DEFICIT—ONE WEEK POSTOPERATIVE VS. PREOPERATIVE BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)
L. S.	?	500	572	451	121	+991	+906	+85	+919	+755	+164
D. B.	125	500	772	380	392	+219	+255	−36	−53	+175	−228
D. T.	500	1000	2250	1287	963	+1418	+1165	+253	+168	+478	−310
J. P.	540	500	1452	696	756	+761	+588	+173	−191	+192	−383
J. H.	500	500	695	348	347	−476	−62	−414	−671	−110	−561
AVERAGE (5 patients)		600	1148	632	516	+582	+570	+12	+34	+298	−264
AVERAGE (4 patients)	736	625	1292	678	614						

*According to weighed sponge technique.

TABLE VIII. WEDGE RESECTION

PATIENT	ESTIMATED* LOSS AT OPERATION BLOOD (C.C.)	GIVEN AT OPERATION BLOOD (C.C.)	ACTUAL LOSS AT OPERATION BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	GAIN OR LOSS—FIRST POSTOPERATIVE WEEK BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)	EXCESS OR DEFICIT—ONE WEEK POSTOPERATIVE VS. PREOPERATIVE BLOOD (C.C.)	PLASMA (C.C.)	CELLS (C.C.)
R. A.	1950	2000	2886	1356	1530	+1441	+1306	+135	+555	+1150	−595
E. F.	?	1000	465	310	155	−517	−157	−360	+18	+133	−115
V. M.	100	500	862	484	378	+656	+653	+3	+294	+469	−175
S. S.	800	1000	688	316	372	−18	+294	−312	+294	+578	−284
A. M.	1000	1000	657	5	652	+297	+228	+69	+640	+823	−183
G. P.	600	1000	1341	644	697	+686	+615	+71	+345	+571	−226
J. V.	305	500	300	50	250	+429	+313	+116	+629	+563	+66
J. H.	400	500	623	281	352	+970	+1080	−110	+837	+1099	−262
AVERAGE (8 patients)		937	979	431	548	+493	+542	−49	+452	+673	−221
AVERAGE (7 patients)	736	929	1052	448	604						

*According to weighed sponge technique.

The Tables which follow, IX through XII, summarize the blood losses during various pulmonary resections, the estimated losses, blood replacement, the additional blood lost in the first postoperative week and present a comparison of the status of the blood volumes preoperatively and one week postoperatively.

TABLE IX. BLOOD LOSS DURING VARIOUS PULMONARY RESECTIONS

OPERATION	NO. OF PATIENTS	MAXIMUM (C.C.)	MINIMUM (C.C.)	AVERAGE (C.C.)	PLASMA (C.C.)	CELLS (C.C.)
Segmental resection	44	3294	314	1759	950	809
Lobectomy	8	3728	639	1870	1100	770
Local enucleation	5	2250	572	1148	632	516
Wedge resection	8	2886	300	979	430	549

These figures indicate that the average blood loss during excisional pulmonary surgery is large and in certain patients it may be extremely so, amounting in some cases in this series to over 70 per cent of the patient's total blood volume. The greatest individual blood losses as well as the highest average losses occurred in patients in whom anatomical resection of a lobe or a segment was performed, while smaller losses were encountered in patients treated by localized excisions. The losses in plasma and red-blood cells were generally in the normal proportions. The large average losses in these thoracic surgical patients are comparable for similar operations to those reported by Forsee,[4] Baronofsky,[3] Thomas,[7] Berlin,[9, 10] Miller,[11] and their associates, and by White and Buxton.[8]

TABLE X. AVERAGE ESTIMATED BLOOD LOSS, BLOOD REPLACEMENT, ACTUAL LOSS, AND P.O. DEFICITS

	SEGMENTAL RESECTION (C.C.)	LOBECTOMY (C.C.)	LOCAL ENUCLEATION (C.C.)	WEDGE RESECTION (C.C.)
Gravimetrically estimated loss	891	1214	416	736
Average given by tranfusion	1251	1500	600	937
Actual loss	1759	1870	1148	979
Postoperative deficits: Blood	-508	-370	-548	-42
Plasma	-200	-200	-272	+132
RBC	-308	-170	-276	-174

The figures in Table X demonstrate the deficiencies of the gravimetric method of determining blood loss during surgery. Although the amount given by transfusion exceeded the estimated loss in every case, averaging between 25 and 30 per cent more, there was a significant average postoperative deficit in each group of patients. In the segmental resection group, only 71 per cent of the blood lost during surgery was replaced and over 60 per cent of the deficit was due to red cells. Eighty per cent of the operative blood loss was replaced in the lobectomy patients, the 5 local enucleation patients received only 52 per cent replacement, while the 8 patients who underwent wedge resections showed a postoperative deficit of only 42 c.c. and the postoperative blood volume was 99 per cent of the preoperative value. The deficiency in red-blood cells predominated in all patient groups. This was particularly striking in the patients who had wedge resections. These patients showed an average immediate postoperative plasma volume 132 c.c. greater than the pre-

operative value, but their red cells decreased an average of 174 c.c., the loss in erythrocytes accounting for 100 per cent of the 42 c.c. diminution in total blood volume. These observations agree with those of Stanton,[6] Foree[4] and others who have found that blood replacement on the basis of gravimetric estimations of loss results in undertransfusion to the extent of about 40 per cent. The fact that the postoperative deficit in erythrocytes generally exceeds that of plasma is interesting and important.

TABLE XI. AVERAGE BLOOD VOLUME CHANGES IN THE FIRST POSTOPERATIVE WEEK

	SEGMENTAL RESECTION (C.C.)	LOBECTOMY (C.C.)	LOCAL ENUCLEATION (C.C.)	WEDGE RESECTION (C.C.)
Blood volume gain first P.O. week	388	261	582	493
Plasma volume gain first P.O. week	477	498	570	542
RBC loss or gain first P.O. week	-89	-237	12	-49

Table XI reflects the changes in the average blood volume in the various groups of patients in the week following operation. Thirty-eight of the 44 segmental resection patients showed an increase in blood volume during the first postoperative week and this increase averaged 388 c.c. The plasma volume increased in 39 patients and the average plasma volume gain in the entire group was 477 c.c. Nineteen of these patients showed an increase in the red-cell volume during this period but there was a decrease in 25 patients. Those with an increase had an average gain of 112 c.c. while 25 patients exhibited an average loss of 242 c.c. The average loss in the whole group was 89 c.c. per patient. The 8 lobectomy patients showed an average blood volume gain of 261 c.c. during the first postoperative week. There was an increase in 5 patients and a decrease in 3. The entire gain in blood volume was due to an increase in the plasma, which amounted to an average of 498 c.c., while there was a simultaneous average loss of 237 c.c. of red cells. The local enucleation patients gained an average of 582 c.c. in blood volume during the first postoperative week, this increase being due almost solely to an average plasma gain of 570 c.c. The red cells showed an average increase of only 12 c.c. A loss of 36 c.c. and 414 c.c. of cells occurred in 2 patients, while the remaining 3 gained 85, 173, and 253 c.c. of erythrocytes. The 8 patients who had wedge resections gained 493 c.c. in average blood volume during the first postoperative week and again this increase was contributed solely by the plasma. The plasma volume increased 542 c.c. during this period but the red-cell volume decreased an average of 49 c.c. The results of these studies confirm the investigations of Thomas,[7] Forsee,[4] and Lyon,[5] and others who found that while the plasma volume shows a rather rapid return toward normal in the early postoperative period, a continuing loss of red-blood cells occurs during this interval.

The figures in Table XII demonstrate an excellent status of the blood volume at the end of the first postoperative week as compared with the preoperative values. The segmental resection and lobectomy patients were only 120 c.c. and 109 c.c., respectively, below their preoperative volumes, while the local enucleation group exhibited an increase of 34 c.c. and the wedge resection patients had gained 452 c.c. However, when these changes are broken down

TABLE XII. AVERAGE DIFFERENCES BETWEEN THE PREOPERATIVE BLOOD VOLUME AND THE BLOOD VOLUME AT THE END OF THE FIRST POSTOPERATIVE WEEK

	SEGMENTAL RESECTION	LOBECTOMY	LOCAL ENUCLEATION	WEDGE RESECTION
	(C.C.)	(C.C.)	(C.C.)	(C.C.)
Blood Vol.; first P.O. week vs. Preop.	-120	-109	34	452
Plasma Vol.; first P.O. week vs. Preop.	277	298	298	673
RBC Vol.; first P.O. week vs. Preop.	-397	-407	-264	-221

into plasma and red cells, the situation does not appear so favorable. Those patients who had a segmental resection had an average plasma volume which exceeded their preoperative figure by 277 c.c., but they showed an average red-cell decrease of 397 c.c. Thirty-five patients had a plasma volume at the end of one week which was greater than that preoperatively and only 9 had volumes which were less. In contrast, 39 of 44 patients had red-cell volumes at the end of the first postoperative week which were less than their preoperative volumes, while an increase occurred in only 5. The average red-cell volume one week postoperatively was 2,077 c.c. in comparison with the preoperative volume of 2,474 c.c. Since the immediate postoperative deficit was 308 c.c., it is apparent that the majority (78 per cent) of this 397 c.c. deficit was due to inadequate replacement of blood at the time of operation. Essentially the same changes occurred in the lobectomy patients. Although the plasma volume at the end of the first postoperative week exceeded the preoperative value by 298 c.c., the red-cell volume was 407 c.c. less. One hundred seventy cubic centimeters (42 per cent) of this deficiency was due to underreplacement at the time of surgery, while an additional 237 c.c. of red cells were lost during the first postoperative week. The red-cell losses in the local enucleation and wedge resection patients were not as great as in the patients with more extensive operations, but they were substantial. The 34 c.c. increase in average blood volume in the local enucleation patients during the first postoperative week, as compared with their preoperative value, was accomplished by an average plasma volume increase of 298 c.c. while the red-cell volume was decreased 264 c.c. Since these patients showed an immediate postoperative deficit of an average of 276 c.c. of red cells, this deficiency could be completely accounted for, on the average, by underreplacement of blood during surgery. The red-cell volume of the 8 patients who had wedge resections averaged 221 c.c. less at the end of the first postoperative week than preoperatively but the plasma volume had increased 673 c.c. during the same interval, accounting for an increased blood volume of 452 c.c. In view of the fact that the average immediate postoperative red-cell deficit in these patients was 174 c.c., 78 per cent of the decrease at the end of the first postoperative week was due to too little blood at the time of surgery. The significance of these deficits in red cells at the end of the first postoperative week becomes apparent when it is appreciated that the persisting deficit in the most favorable group of patients (local enucleations) amounted to the quantity of red cells normally contained in slightly over a pint of whole blood (about 10 per cent of the normal blood volume), while the least favorable group (lobectomies) showed a diminution equivalent to the red cells in two pints of whole blood or about 20 per cent of the normal blood volume.

SUMMARY

1. The blood volume changes in 65 patients who underwent pulmonary resections are presented.

2. The blood loss during intrathoracic operations is large and replacement on the basis of gravimetric estimations of loss results in significant under-transfusion. The deficit averages about 40 per cent of the total blood loss.

3. Restoration of the total blood volume toward normal during the first postoperative week is accomplished by an increase in the plasma fraction. There is a continued loss of red cells during this period.

4. In most patients the red-cell deficit at the end of the first postoperative week is due largely to inadequate replacement of blood lost during surgery.

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DISCUSSION

DR. ARTHUR M. VINEBERG, Montreal, Quebec.—I should like to take this opportunity to discuss Dr. Storey's paper, and to congratulate him on his excellent work. We have been particularly interested in blood volume studies, because patients with coronary artery insufficiency can quite easily be thrown into pulmonary edema by a sudden increase of blood volume. Recently, however, we have had occasion to make use of blood volume studies in the preparation of two patients with mitral stenosis for operation. One of these patients had been under observation and medical treatment for at least four months. Low salt diet, diuretics, etc., failed to prepare these patients to a point where it was safe for them to undergo surgery. A study of the blood volume in both these cases indicated that it was augmented by approximately 50 per cent. In each case, whole blood was removed and packed red blood cells were reintroduced into the circulation. In each case, this resulted in dramatic improvement of the patient's right heart failure; ascites, liver enlargement, and orthopnea markedly decreased. Both of these patients were operated upon in the right lateral horizontal position, without the use of refrigeration. There was no difficulty.

INDUCED CARDIAC ARREST FOR INTRACARDIAC SURGICAL PROCEDURES

An Experimental Study

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THE ability of the heart to survive circulatory interruption might be increased by removing the necessity for it to continue beating in the face of a diminished blood supply. When the venae cavae are occluded, the coronary blood flow is abruptly curtailed while ventricular systolic contractions persist. When this situation is prolonged, as in open heart operations with the aid of hypothermia, the discrepancy between blood supply and muscular activity may be accentuated. With this in mind, a series of experiments were done to determine if the heart could be deliberately stopped while its blood supply was obstructed and then restarted again, and if recovery was thereby aided.

We were familiar with the unsuccessful attempts of Björk[1] at inducing reversible cardiac arrest by local freezing of the heart and by injections of acetylcholine. Niazi and Lewis[2] demonstrated the ability of the rat heart to survive prolonged periods of cardiac arrest which occurred at temperatures in the vicinity of 5.0° C. Senning[3] and Glenn and Sewell[4] induced ventricular fibrillation in dogs while perfusing the body with an extracorporeal circuit. They demonstrated that prolonged periods of fibrillation were tolerated under these conditions with survival, and emphasized the advantage of the nonbeating heart in avoiding entrance of air into the coronary arteries.

A method was developed of suddenly stopping the normal heartbeat which was consistent and reversible. This consists of rapidly perfusing the coronary system with a 5 per cent solution of potassium chloride. With the acending aorta compressed, 1 c.c. per kilogram of body weight is injected into the cavity of the left ventricle. Manually squeezing the ventricles aids entrance of the solution into the coronaries. Usually ventricular activity ceases in about 30 seconds. The still heart may then be manipulated or incised. Following completion of the surgical procedure, the heart may be started again by simple massage. As the coronary circulation is manually restored, the potassium chloride is washed out and diluted in the blood stream. The heart which is flaccid at first regains its tone and then usually goes through a phase of coarse fibrillation

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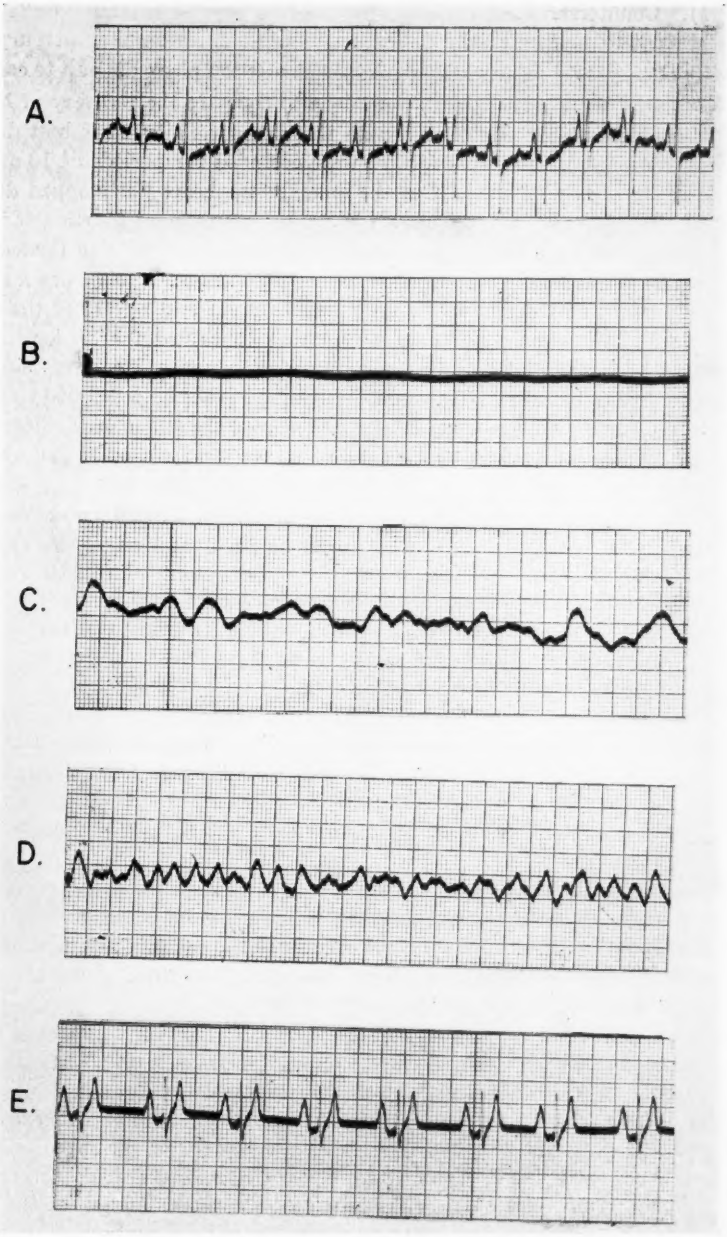

Fig. 1.—Electrocardiogram Lead II from dog at normal temperature. *A*, Normal beat. *B*, Arrested with potassium chloride. *C*, Coarse fibrillation with massage. *D*, Fibrillation just prior to use of countershock. *E*, Resumption of normal rhythm. Evidence of hyperpotassemia.

(Fig. 1). Countershock readily converts this to a regular rhythm. Calcium is not necessary to neutralize the potassium chloride for resuscitation purposes. In fact, it proves troublesome by making the fibrillation phase difficult to control.

A series of acute experiments were done to compare the recovery of hearts stopped during vena caval occlusion with that of hearts allowed to beat during the occlusion period. The venae cavae were occluded for periods of 10 and 12 minutes in 20 dogs. In one-half of the animals, the heart was stopped during the occlusion. In each case, the chest was opened in the right fourth interspace under endotracheal ether-oxygen anesthesia. The azygos vein was ligated and the venae cavae occluded with snares. In most animals an incision was made in the right atrium. After closure of the atrial incision and release of the caval snares, resuscitative measures were begun and continued for as long as 20 minutes, if necessary. These consisted of cardiac massage, countershock, and, in some animals, intraventricular epinephrine, 0.25 c.c. of a 1:1,000 solution. At 30 minutes, following release of the caval snares, the status of the heart was evaluated by direct inspection and by recordings of the ventricular and arterial pressures.

Of the hearts allowed to beat during the occlusion, 9 of 10 had ventricular fibrillation when the caval snares were released. Regular rhythm was restored with countershock in all but one heart. After restoration of regular rhythm, injection of epinephrine was needed in every case because of hypotension. This produced a rise in blood pressure which was only temporary. The average systolic blood pressure, 30 minutes after release of the caval snares, was 72 mm. Hg. The average time of onset of regular beats was 8 minutes.

Of the 10 arrested hearts, 9 were restored to regular rhythm. The average time of onset of coordinated beats following release of the caval snares was 8.5 minutes. Epinephrine was needed in one-half of the cases. Its effect was quite different from that in the other group, however, in that the blood pressure increase was sustained. The average systolic blood pressure at 30 minutes was 135 mm. Hg (Fig. 2).

These experiments seemed to indicate that the stopped heart had a slightly better tolerance of circulatory occlusion. Because of the brain damage occurring with lengthy interruption of the circulation at normal temperatures, of course, no long-term observations were possible. Therefore, survival experiments were done using hypothermia to protect the brain.

Dogs under ether-oxygen anesthesia were cooled in ice water. At rectal temperatures of 26° C., the heart was stopped for from 10 to 20 minutes in a series of dogs in which atrial and ventricular septal defects were produced and repaired. Large defects were cut out of the interatrial septum and were closed with pedicled flaps of the right atrial wall which were in turn replaced with pedicled pericardial flaps. Ventricular septal defects were made through incisions in the right ventricular wall and closed by approximation of the edges of the defect with silk sutures. The performance of these operations on a completely quiet and bloodless heart was relatively simple. No difficulty was encountered with air embolism of the coronary arteries. Of 14 dogs in which technically satisfactory procedures were carried out, 12 survived operation and

rewarming (40° C. warm water bath). Nine were completely well for a week or more, and 6 continue well about four months or more postoperatively. One-half of these represent ventricular and half atrial septal defect repairs.

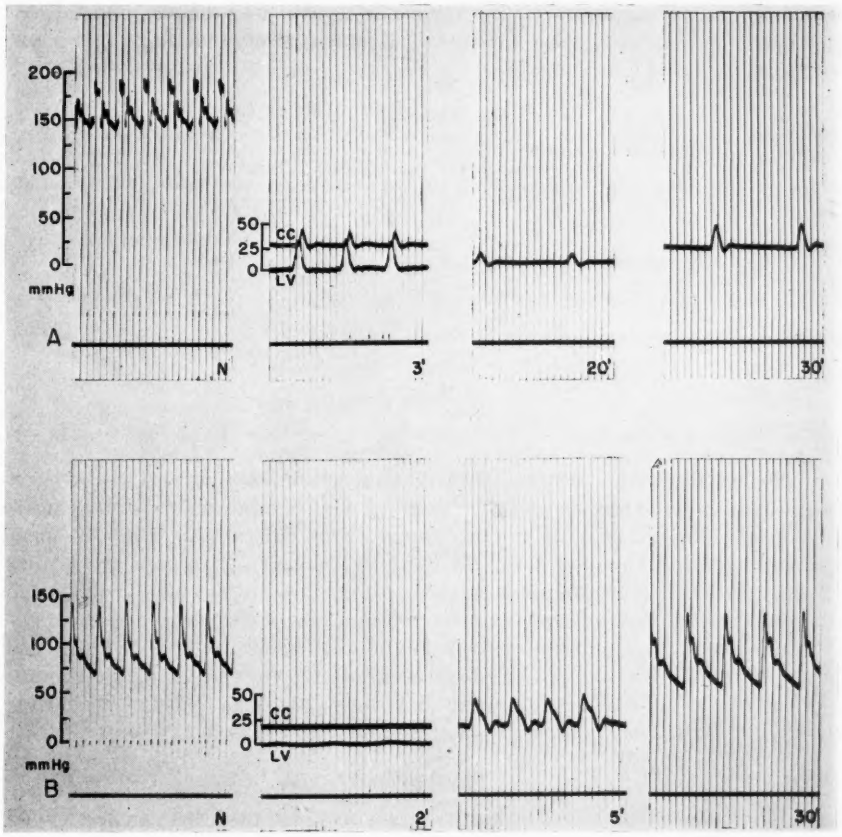

Fig. 2.—*A*, Blood pressure curves before, during, and at 20 and 30 minutes after 12 minutes of caval occlusion. Heart allowed to beat during occlusion. *B*, Before, during, and at 5 and 30 minutes after caval occlusion with induced cardiac arrest. These represent extremes in the experiments done at normal temperatures, but illustrate the trend of the results.

When the rectal temperature was lowered to 22° C., it was possible to arrest the heart for 30 minutes with complete recovery of the animal. A group of 20 dogs were subjected to right atrial cardiotomy under these conditions. Fifteen dogs survived for a week or more postoperatively without evidence of cardiac or central nervous system damage. Recovery was prompt and no ill effects attributable to the potassium chloride were seen. Regular rhythm could not be restored in 1 animal. Two succumbed during rewarming. Three died in two to six days after initially recovering. These 3 animals required repeated countershocks during resuscitation. Histologic sections of their hearts showed coagulation necrosis and focal hemorrhages beneath the epicardium.

In order to compare these results with those from other techniques, a control series of 30 dogs was subjected to circulatory occlusion at 22° C. for 30 minutes. In 10 dogs the venae cavae were occluded. In 10, both the venae cavae and the aorta and pulmonary artery were occluded. In the other 10, the venae cavae were occluded and the right ventricle then stimulated with an inductorium current to induce ventricular fibrillation. The results of these experiments are compared in Table I.

TABLE I. CIRCULATORY OCCLUSION 30 MINUTES AT 22° C.

	NUMBER OF DOGS	INTRACTABLE FIBRILLATION	REWARMING DEATH	POSTOPERATIVE DEATH	SURVIVORS	PER CENT
Induced cardiac arrest	20	1	2	2 (1 and 6 days)	15	75
Induced fibrillation	10	1	0	3 (36 hours)	6	60
Caval occlusion	10	0	1	2 (24 hours)	7	70
Caval and outflow occlusion	10	0	1	3 (1 and 7 days)	6	60

The survival rates were similar no matter what technique was used. Four dogs with caval occlusion and 6 with caval and outflow occlusion developed ventricular fibrillation. All of these animals were defibrillated, although some required multiple countershocks. In the latter category, 2 in each group died during the first twenty-four hours postoperatively with histologic evidence of thermal damage to the heart. One dog in each group died during rewarming. Of the animals in which ventricular fibrillation was induced, only 1 had intractable fibrillation when the countershock was used at the end of the 30 minute period. Three animals in this group died during the first 36 hours postoperatively, all of which had multiple countershocks.

DISCUSSION

It is astonishing at first to see the ease with which the heart can be stopped and then started again after prolonged arrest. The technique of potassium chloride injection is a modification of the early defibrillation method developed by Hooker[5] and Wiggers.[6] Restoration of the normal beat seemed to be no more difficult in those animals which had ventricular incisions, although no controlled studies were done to determine the soundness of this impression. The similarity in the results of the control experiments for circulatory occlusion of 30 minutes at 22° C. was somewhat surprising, particularly in the group with induced fibrillation.

SUMMARY

The deliberate production of cardiac arrest for the purpose of opening the heart surgically was found to be possible with recovery. The heart was stopped with the injection of potassium chloride into the left ventricle. Resumption of

the normal heartbeat was obtained by massage of the heart and electrical countershock. With the aid of hypothermia, cardiac arrest for periods of 10 to 30 minutes was induced and intracardiac operations carried out with recovery of the animals. Controlled experiments of circulatory occlusion for 30 minutes at 22° C. demonstrated virtually no difference in survival rates when the heart was allowed to beat, stopped, or even made to fibrillate during the entire period of occlusion.

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Discussion

DR. RALPH ADAMS, Boston, Mass.—Approximately ten people have inquired of me concerning the fate of a 10-year-old child whom I mentioned before this Association a year ago. At that time, he was alive four days after surviving one hour and fifty minutes of ventricular fibrillation, and currently then had lower nephron necrosis.

I am pleased to report that the child apparently is now normal in all respects and does his schoolwork and other activities as a healthy boy should.

Subsequently, a patient with coarctation of the thoracic aorta had ventricular fibrillation for seventy minutes, and has recovered and is all right. He did not have any renal symptoms, which has made me wonder if there was some kidney protection afforded by the chronic deficiency of circulation below the coarctation.

OPEN LEFT HEART SURGERY IN DOGS DURING HYPOTHERMIC ASYSTOLE WITH AND WITHOUT EXTRACORPOREAL CIRCULATION

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ALTHOUGH the body temperature of dogs can be rapidly lowered to the terminal degree of about 16° C.[1] and the animals successfully resuscitated by immersion in warm water,[2] this extreme condition cannot be fully utilized for open intracardiac surgery[3] since the high mortality due to anoxia and ventricular fibrillation prohibits any human application. Therefore, the most satisfactory clinical results have been achieved at about 25° C. with a safe cessation of circulation of about 5 to 8 minutes.[4, 5]

Attempts have been made to lower the terminal temperature of dogs by substituting a pump-oxygenator for the function of the failing heart[6, 7] and although 1 dog survived a body temperature of 12° C., all other animals died in shock of unknown origin. By circulating, oxygenating, and refrigerating venous blood in a gas dispersion pump-oxygenator,[8] it has been possible to achieve survival of dogs after cardiac arrest of one hour's duration during hypothermia of 0° C.[9] Thus, the use of such biomechanical equipment as a research tool for physiologic investigations has produced a condition which does not have to be fully utilized for the short-term applications of open intracardiac surgery.

In about 40 minutes of blood cooling, the temperature inside the right heart is lowered to about 5° C., and in 15 minutes of bloodwarming, it is raised to 27° C. The differential hypothermia[10] between the upper and the lower part of the body reaches 20° C. As the temperature inside the heart reaches about 13° C., the last contraction is recorded and the heart remains in hypothermic asystole as long as this low temperature is maintained. On rewarming, the heart starts to beat in normal rhythm and at about 28° C. the pump-oxygenator can be turned off. Such a procedure lends itself in a most advantageous way to prolonged intracardiac surgery under direct vision[11] since greater technical accuracy is attainable if the motions of the lungs and of the heart are arrested. By the cannulation of peripheral blood vessels only, the surgical procedure is shortened and trauma to the great vessels in the chest is avoided. At no time during the experiment does the nervous system, the heart, or the viscera suffer from anoxia or from carbon dioxide retention and therefore no time limit is set

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for the careful exploration and repair of intracardiac lesions. Because of the low oxygen consumption of the cold and inactive myocardium, the coronary flow can be drastically reduced, resulting in a bloodless operating field. Special precautions against air embolism are not required since the heart in arrest ejects neither blood nor air into the aorta. In a series of 13 consecutive experiments with left cardiotomies, 9 animals survived the procedure without any clinically detectable ill effect and were sacrificed after an observation period of one month. Four dogs died of postoperative complications such as infection, thrombosis, and hemothorax.

These studies led to the conclusion that large nonhibernating mammals can survive the lowering of their body temperature to or close to the freezing point of water, just like the small nonhibernating rat,[12] if the function of the heart is substituted by a mechanical device. Furthermore, the absence of ventricular fibrillation was surprising and could have been due to the relief of the work load of the heart by the pump-oxygenator or by the pretreatment with quinidine.[13, 14] The effect of carbon dioxide on cardiac rhythm,[15] and the prevention of ventricular fibrillation in dogs during profound hypothermia of 7° to 12° C. by the addition of carbon dioxide to the inspired air,[16] indicate that the exclusion of the heart by a pump-oxygenator is not necessary for the production of hypothermic asystole. We assumed, therefore, that the pretreatment with quinidine must have been the only important factor in the production of hypothermic cardiac arrest without ventricular fibrillation.

Seventy-six dogs were anesthetized with Nembutal and given 30 to 40 mg. of quinidine per kilogram of weight in 200 c.c. saline solution by slow intravenous drip, before being immersed in ice water. Shivering was controlled with small amounts of Pentothal sodium and, when the respiration started to become depressed, hyperventilation with oxygen was started. At body temperatures of 18° to 13° C., as measured in the thoracic esophagus, cardiac standstill or very infrequent beats were recorded and in no instance did ventricular fibrillation develop. Nevertheless, only 8 to 10 per cent of these animals were long-term survivors. Even in cases with very short interruption of the circulation and successful re-establishment of cardiac function during rewarming, the animals succumbed in delayed shock the next day.

The following attempts were made to overcome this difficulty. Differential hypothermia was produced by clamping the thoracic aorta and by cooling of the pulmonary circulation with refrigerated oxygen. In 13 dogs, the temperature gradient amounted to only 2° to 6° C.

In 12 dogs, the heart was arrested at a body temperature above 20° C. by cold or iced saline solution.

A simpler method to achieve cardiac standstill was used in 22 animals by intracoronary perfusion of potassium chloride[5, 17] followed by intracardiac calcium before resuscitation of the heart.

An artificial pacemaker was employed in 8 dogs,[18, 19] and hypotension, bradycardia, and arrest could be interrupted and the temperature lowered for an additional 3° C. during 15 minutes of stimulation. The artificial pacemaker was not efficient in the rewarming period.

Selective rewarming of the heart was attempted by diathermy,[20] by warm saline solution, and by a heating element in the esophagus.[21]

None of these procedures listed affected in any way the high mortality of dogs after short cessation of the circulation during hypothermia below 20° C. At present, the only clue to a possible solution for this difficulty, though not elucidation of the problem, lies in the administration of cortisone. After preliminary testing of various dosages in 12 dogs, the following schedule appears to be satisfactory. The day before the experiment the animals receive 100 mg. cortisone acetate intramuscularly; 100 mg. hydrocortisone intravenously before cooling; and 50 mg. cortisone acetate intramuscularly at night and during the following three days. Instead of water, the animals are given saline solution to drink.

The actual experimental procedure consists in a right thoracotomy at the time the heart rate has slowed down to about 16 beats per minute at about 20° C. When both caval and azygos vein are occluded, the temperature has drifted to 14° C. in the smaller animals and the heart is almost in standstill. After release of the venous occlusion, hyperventilation with oxygen is started again, the body is rewarmed by dry heat, and gentle massage of the heart is started to prevent dilatation of the right heart at such low temperatures. At first the femoral blood pressure does not have to exceed 20 to 30 mm. Hg, but when the temperature has risen to about 21° C. a higher blood pressure is desirable and at that time a remarkable increase in myocardial tonus can be achieved by a slow intravenous drip of 20 mg. of l-Arterenol in 500 ml. of a plasma expander. This unusually high concentration is chosen in order to derive the benefit of l-Arterenol without overloading the circulation. Even a comparatively small increase in blood volume at that stage will invariably cause pulmonary edema. When the heart rate has reached at least 30 beats per minute at about 22° to 23° C. the massage can be discontinued. The slow drip of plasma expander and l-Arterenol is continued throughout the slow rewarming procedure which takes four to five hours. Above 32° C. spontaneous respiration becomes dependable enough to stop the respirator, but oxygen is administered through the tracheal tube until the animal is awake.

In seven consecutive experiments (Table I), the circulation was interrupted from 10 to 15 minutes at temperatures from 18° to 14° C. The 2 dogs with a 15 minute inflow occlusion did not wake up; the 2 animals with 12 minute

TABLE I. VENOUS INFLOW STASIS DURING SEVERE HYPOTHERMIA IN CORTISONE-TREATED DOGS

DOG NO.	WEIGHT (KILOGRAM)	TEMPERATURE (DEGREES CENTIGRADE)	HEART RATE (PER MINUTE)	DURATION INFLOW STASIS (MINUTES)	CARDIAC MASSAGE (MINUTES)	OUTCOME
1	7.3	14.0	2	15	38	Died
2	8.6	14.5	6	10	32	Lived
3	10.0	16.0	12	10	15	Lived
4	10.0	18.5	10	10	12	Lived
5	11.0	18.0	16	12	29	Lived
6	6.0	15.0	4	15	22	Died
7	10.0	16.5	12	12	24	Lived

inflow occlusion survived, but both still seemed to be under the effect of the narcotic the following day. This series is much too small to make a definite statement about the ultimate advantages of inducing profound hypothermia per se, but it appears as if the safe period of circulatory interruption cannot be extended beyond 12 minutes at body temperatures of 14° C.

SUMMARY

1. Differential hypothermia of 0° C. can be produced in dogs if the venous return is circulated, oxygenated, and refrigerated in a small, plastic pump-oxygenator. This condition provides a bloodless field for prolonged open intracardiac surgery without the complications of anoxia, air embolism, or ventricular fibrillation.

2. Hypothermic cardiac arrest can also be achieved without extracorporeal circulation by the prevention of ventricular fibrillation with quinidine. Delayed shock following a severe anoxic insult at body temperatures below 20° C. can be prevented and treated by the vigorous administration of cortisone. At present, it seems unlikely that the absolutely safe period of inflow stasis could be materially prolonged beyond 12 minutes at the temperatures employed, and therefore even severe hypothermia without extracorporeal circulation may aid in simple and short intracardiac surgery only.

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Discussion

DR. FLOYD J. LEWIS, Minneapolis, Minn.—I should like to congratulate Dr. Gollan on his impressive use of a small heart-lung machine to extend the range of hypothermia in these animals, but I particularly want to comment on his attempts to reach these lower temperature ranges without the small heart-lung machine. We are interested in the same problem. As you will remember, he was able to achieve cardiac standstill in most of his animals cooled to temperatures below 12° or 10° C. by giving them quinidine beforehand, and he encountered almost no ventricular fibrillation. My associate, Dr. Niazi, has not been able to achieve standstill in such a high percentage of dogs but when he has achieved it most of them have recovered, so I thought it would be worth while to mention the method that Dr. Niazi has used in the laboratory. There are a number of involved experiments and I will comment only on one type, in which dogs from 3 to 6 months of age, weighing around 20 pounds, were cooled while breathing 5 per cent carbon dioxide. When the temperature got down to about 20° C., the carbon dioxide was stopped and they then shifted from slight acidosis into alkalosis, and at a lower temperature 17 out of 38 went into cardiac standstill. This was the end we were trying to achieve. Those 17 were all cooled below 10° C. Finally they were rewarmed and 13 of the 17 are long-term survivors. So there is nothing intrinsic in these low temperatures that will result in late shock, such as Dr. Gollan found in his dogs that were cooled without the heart-lung machine.

(The Surgical Forum papers will be concluded in the December issue.)

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Thirty-sixth Annual Meeting of the American Association for Thoracic Surgery will be held May 7, 8 and 9, 1956, in Miami Beach, Florida. Headquarters will be at the Hotel Fontainebleau.

Requests for Hotel Reservations

These should be mailed directly to Mr. Jack Slone, Director of Sales, Hotel Fontainebleau, Miami Beach, Florida. Please mention this Association, the type of accommodation desired, the date and approximate hour of arrival and departure. If accommodations are desired elsewhere in Miami Beach, please communicate directly with the hotel of your choice.

Thoracic Surgical Forum

The Thoracic Surgical Forum will be continued as a special session at the 1956 meeting. The Forum is primarily for the presentation of short papers on current thoracic research, experimental problems, anatomical studies and modified or new surgical techniques. The inclusion of any considerable amount of clinical material in these reports makes the choice more difficult and the Program Committee reserves the right to reject such papers, or to suggest their transferral to the Regular Program.

Papers at this session will be limited to ten minutes, including the showing of lantern slides or other illustrative material. At the discretion of the President, three minutes may be allowed as the maximum discussion for each paper.

All Thoracic Surgical Forum papers will be published together in one issue of the JOURNAL. Maximum length: 3000 words without illustrations. If illustrated, an appropriate number of words must be subtracted for each cut used.

Abstracts for Papers

Abstracts for the presentation of all papers at the 1956 meeting must be received on or before Dec. 15, 1955, otherwise they will not be considered by the Program Committee.

Abstracts should be labeled "For Thoracic Surgical Forum," or "For Regular Program." The abstracts should contain from 200 to 250 words and accurately reflect the contents of the completed paper.

Five, repeat, five copies of *each* abstract must be sent to the Secretary of the Association, Dr. Paul C. Samson, 3959 Happy Valley Road, Lafayette, California. They should not be sent to the Editor.

Those on the program are reminded that papers presented at the meeting *must* be handed to the secretary immediately after their presentation. If they are not ready at that time there is a chance that they will not be published in the JOURNAL OF THORACIC SURGERY.

Motion Picture Session

Provisions have been made to show a limited number of motion pictures to be selected on a competitive basis. *The films themselves,* together with descriptive material concerning length of presentation, etc., must be received by Dr. Julian Johnson, University Hospital, 3400 Spruce St., Philadelphia 4, Pa., before Dec. 15, 1955.

(Continued on next page.)

It is planned to run the motion pictures in a smaller room at the same time as the scientific sessions. If the films are well labeled, it will not be necessary for the author to be present for comment.

Applications for Membership

Applications for Associate Membership in the Assocation must be received by the Membership Committee not later than Dec. 15, 1955, otherwise, the applications will be deferred for consideration until the 1957 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signatures on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Dr. O. T. Clagett
Chairman of the Membership Committee
Mayo Clinic
Rochester, Minn.

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Membership Committee should their applicants be held over for reconsideration a second year.